PROCEEDINGS

OF THE

NEW YORK

PATHOLOGICAL SOCIETY

FOR THE YEAR 1896

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1897

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LIST OF OFFICERS AND COMMITTEES FOR THE YEAR 1896.

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* Dr. John A. Swett,	1844
* Dr. Willard Parker,	1845, 1846, 1847
* Dr. James R. Wood,	1848, 1857
Dr. T. M. Markoe,	1850 1879
* Dr. W. H. Van Buren,	1850
* Dr. Charles E. Isaacs,	1851
Dr. John T. Metcalfe,	1852
* Dr. Henry Van Arsdale,	1853
* Dr. Jackson Bolton,	1854, 1855
* Dr. Robert Watts,	1856
* Dr. Edmund R. Peaslee,	1858
* Dr. John C. Dalton,	1859
* Dr. Alfred C. Post,	1861
* Dr. Thomas C. Finnell,	1862
* Dr. David S. Conant,	1863
Dr. Abraham Jacobi,	1864
* Dr. Gurdon Buck,	1865
* Dr. Henry B. Sands,	1866
* Dr. William B. Bibbins,	1867
* Dr. Ernest K. Krackowitzer,	1868
Dr. L. A. Sayre,	1869
* Dr. Joseph C. Hutchinson,	1870
* Dr. A. L. Loomis,	1871, 1872
* Dr. Erskine Mason,	1873
Dr. Herman Knapp,	1874
Dr. Francis Delafield,	1875
Dr. Charles K. Briddon,	1876
Dr. Edward G. Janeway,	1877
* Dr. John C. Peters,	1878
Dr. Edward L. Keyes,	1879
Dr. T. E. Satterthwaite,	1880, 1881
Dr. E. C. Seguin,	1882

* Deceased.

Dr. George F. Shrady,	1883, 1884
Dr. John A. Wyeth,	1885, 1886
Dr. T. Mitchell Prudden,	1887
Dr. W. P. Northrup,	1888, 1889
* Dr. J. West Roosevelt,	1890
Dr. Herman M. Biggs,	1891
Dr. H. P. Loomis,	1892, 1893
Dr. G. C. Freeborn,	1894
Dr. George P. Biggs,	1895
Dr. John Slade Ely,	1896

SECRETARIES.

* Dr. William C. Roberts,	1844 to 1849
* Dr. H. D. Buckley,	
* Dr. Henry G. Cox,	1850 to 1852
* Dr. William Henry Church,	1852
* Dr. Charles M. Allen,	1852 to 1853
* Dr. George T. Elliott,	1853 to 1854
* Dr. J. FosterJenkins,	1854 to 1855
* Dr. E. Lee Jones,	1855 to 1861
Dr. T. Gaillard Thomas, *pro tem.*,	1855
Dr. Henry D. Noyes, *pro tem.*,	1858
Dr. George F. Shrady,	1861 to 1879
* Dr. Wesley M. Carpenter,	1880 to 1888
Dr. Walter Mendelson,	1889
Dr. T. L. Stedman,	1889 to 1891
Dr. Ogden C. Ludlow,	1891 to

LIFE MEMBERS.

Blumenthal, Mark,	1861	Markoe, T. M.,	1847
Bradley, E.,	1865	Newman, R.,	1864
Draper, W. H.,	1858	Packard, Charles W.,	1858
Eliot, Ellsworth,	1855	Purdy, A. E. M.,	1866
Emmet, T. Addis,	1853	Sayre, L. A.,	1847
Hinton, John H.,	1856	Shrady, George F.,	1858
Hull, Joseph J.,	1862	* Smith, J. Lewis,	1855
Jacobi, Abraham,	1861	Thomas, T. G.,	1855
Lambert, Edward W.,	1858	Warner, J. W.,	1857

* Deceased.

MEMBERS OF THE SOCIETY.

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Abbott, Frank.
Adams, C. T.
Adams, R. S.
Alexander, Samuel.
Armstrong, S. T.

Bailey, Pearce.
Bang, R. T.
Bangs, L. Bolton.
Barstow, Donald W.
Beach, B. S.
Belcher, Sarah.
Biggs, George P.
Biggs, Herman M.
Bissell, J. B.
Bleything, G. D.
Boldt, Herman J.
Booth, J. A.
Bovaird, David.
Bradley-Byström, Elizabeth N.
Brannan, J. W.
Brickner, Samuel M.
Brooks, Harlow.
Brown, Dillon.
Brown, F. Tilden.
Bruce, C. E.

Cammann, D. M.
Carr, Walter L.
Carter, DeLancy.
Chambers, Potter F.
Cheesman, T. M.
Clark, L. Pierce.
Coleman, Warren.
Collins, Joseph.
Conner, Lewis A.
Cooley, William B.
Crandell, Floyd M.
Culver, J. E.
Currier, Charles G.
Cushier, Elizabeth M.

Dawbarn, R. H. M.
Delafield, Francis.
Delavan, D. Bryson.
Deming, N. L.
Denton, M. P.
Dixon, George A.
Dowd, C. N.
Dunham, E. K.

Edebohls, George M.
Elliot, George T.
Elliott, George R.
Ely, John S.
Ewing, James.

Ferguson, Frank.
Fischer, Charles S.
Fisher, E. D.
Fitzpatrick, Charles B.
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Freeman, R. G.
Fuller, R. N.

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Gibson, C. L.
Grauer, F.

Hamilton, C. S.
Hartley, Frank.
Heiman, Henry.
Heineman, Henry M.
Henry, Nelson H.
Herter, C. A.
Hodenpyl, Eugene.
Holt, L. Emmett.
Huddleston, J. H.
Hudson, Walter G.

Jackson, Frank W.
Jacobi, Mary Putnam.
James, Robert C.
James, Walter B.
Janeway, E. J.
Jeffries, F. M.
Johnson, A. B.
Jones, Mary A. D.
Jones, S. Seabury.
Judson, Adoniram B.

Kilham, Eleanor B.
Kipp, Charles J.
Knapp, Herman.
Knapp, John B.
Kneer, F. G.
Knight, Charles H.
Koerner, C. F.

Lambert, Alex.
Lang, F.
Larkin, John H.
Leale, Charles A.
Leaming, Edward.
LeBoutillier, W. G.
LeFevre, E.
Lewis, Daniel.
Liautard, A. F.
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Lockwood, G. R., Jr.
Loomis, H. P.
Ludlow, O. C.
Lynch, J. B.
Lynde, G. S.

McAlpin, D. H., Jr.
McBurney, Charles
McCreery, John A.
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MacHale, F. S.
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Markoe, J. W.
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Mowry, E. C.
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Nicoll, M., Jr.
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Spitzka, E. C.
Stearns, H. S.
Stedman, T. L.
Stickler, J. W.
Stimson, Daniel M.
Stone, W. S.
Swasey, John H.

Taylor, H. Ling.
Thacher, John S.
Thayer, A. E.
Thelberg, John.
Tuttle, G. A.

Valadier, Charles A.
Van Cott, J. M.
Van Gieson, Ira.
Van Santvoord, Richard.
Van Schaick, George G.
Vissman, William.

Wackerhagen, G.
Waldstein, Louis.
Walker, Henry F.
Walsh, Simon J.
Warrin, M. L.
Weeks, John E.
Wendt, E. C.
Weston, A. T.
Whitman, Royal.
Wiener, R. G.
Wilde, Thomas.
Williams, Anna W.
Wollstein, Martha.
Wright, Jonathan.
Wyeth, John A.
Wylie, W. Gill.
Wynkoop, G. H.

During the Year 1896
the following Members were lost
to the Society through Death

T. H. Burchard
Guido Furman
C. Milne
J. J. Mapes
L. F. Pray
J. H. Ripley
J. West Roosevelt
C. A. Sabine

PROCEEDINGS

OF THE

NEW YORK PATHOLOGICAL SOCIETY.

Stated Meeting, February 12, 1896.

JOHN SLADE ELY, M. D., PRESIDENT.

Dr. IRA VAN GIESON presented a preliminary report on some studies he had made on the explanation of true

HETEROTOPIA OF THE SPINAL CORD.

He said that by heterotopia of the spinal cord was meant a dislodgment of portions of gray matter situated outside of the outlines of the posterior or anterior horns. Pick, in 1878, had first drawn attention to this condition, and had published a case in which he had found exceedingly minute masses of gray matter which had become displaced, and were situated near the middle of the posterior columns. In a second case, published a year or two afterward, he found the same condition, to which he gave the name "heterotopia." After these cases had been placed on record, a number of others had been published, in which all sorts of displacements had been described, but many of these were afterwards found to be really due to bruising of the spinal cord. The speaker said that he had reported two genuine cases, and that, up to the present time, there were only about six cases on record.

The displaced portion was usually situated about the middle of the posterior columns. To understand what he considered to be the true nature of this condition, reference must be made to what are known as "outlying cells." In 1873, Beisso, an Italian, had shown that in the spinal cord of some of the lower animals, particularly in oxen, the ganglion cells were not confined to the gray matter. Sherrington had carefully studied these outlying cells in the human spinal cord. He found that they occurred in three regions, viz.: (1) and most frequently, on the internal surface of the posterior horn; (2) on the outside limb of the posterior horn; and (3) just at the junction of the anterior and posterior horns, where they join the lateral columns. Dr. Van Gieson said that he had found them in a fourth region—in the region of the anterior commissure. In his opinion, heterotopia was simply a clustering together of these outlying ganglion cells. A study of the development of the nervous system showed that this whole system originated from the outer of the three germ-layers—the ectoblast. The first stage of development consisted in a thickening of the dorsal aspect of the embryo, the cells of the ectoblast becoming a little thicker. Next, there was a dipping in of the ectoblast, forming what was called the primitive furrow. This was followed by a slight division between the ectoblast and the primitive furrow. To this the name of "neural crest" had been given, because from these crests arose the spinal ganglia. In the next stage of development, the primitive furrow became deepened and cup-shaped, and the edges of the cup tended to approach each other. A continuation of this process resulted in the formation of a tube—the future canal of the spinal cord. Then the neural crest became spread over the spinal cord, and subsequently divided in two, these halves being situated on the sides of the spinal cord. These lateral halves then spread until they almost reached the anterior portion of the spinal cord. The cells which originally came from the spinal ganglia sent their processes into the spinal cord. As the cells of the primitive medullary canal migrate outwards to

the periphery of the spinal cord, they become pear-shaped, forming the neuroblast, the future ganglion cells. It should be particularly noted that the development of these ganglion cells was in a radial direction. From the radial growth of the ganglion cells and the constant encroachment on the gray matter of the posterior root collaterals and other fibres, some of these cells are thrust out beyond the confines of the gray matter and become the outlying cells; hence these displaced masses of gray matter are simply a grouping together of the outlying ganglion cells—in other words, an exaggeration of a normal condition. Heterotopia is observed, the speaker said, to the greatest extent in those regions in which was to be found the greatest number of outlying cells. The chances of these heterotopic masses forming a nidus for tumors seemed to him extremely small.

TUMORS OF THE BRAIN.

Dr. J. S. THACHER made some remarks on this subject, illustrating them by lantern-slides. He said that tumors of epithelial origin appeared in medical literature much less frequently than formerly. A considerable number of these epitheliomatous tumors had been shown to be sarcomata or endotheliomata. It was natural that true epithelial tumors should not be frequently met with in the brain, because the cells of the nervous system, although originally derived from the epiblast, had so far lost their resemblance to ordinary epithelium that only those growths starting from the lining epithelium of the central canal would show in neoplasms a structure which was distinctly epithelial. Very few cancers of the brain had been reported in recent years. Knapp had collected 40 cases coming under his personal observation, and of the 30 in which the nature of the growth was recorded, not one was cancerous. Dr. M. Allen Starr, in a collection of 269 tumors of the brain, occurring in persons under twenty years of age, and in which the nature of the growth was recorded, found only 10 to be cancerous, and most of these were secondary. The speaker then illustrated

by lantern-slides the nature of the growths found in four cases of primary carcinoma of the brain. These all contained cylindrical cells. Two of them were secondary to tumors elsewhere in all probability; one was in a stage of what could be called properly only epithelioma; and one was a tumor which had apparently begun in the brain and had gone on to multiple metastatic deposits.

The first slide exhibited was from a tumor of the brain secondary to a growth in the stomach. It had been taken from a man, fifty-five years of age, who had come into Dr. Murray's service, at St. Luke's Hospital, complaining of pain in the shoulder. A tumor was found in the scapula which, on examination, proved to be an adeno-carcinoma. Dr. Thacher said that thinking it looked to be secondary to a tumor of the alimentary canal, he had asked if there had been any symptoms pointing in this direction, but he had received a negative reply. During the last two weeks of life the man had complained of pain in his head; the right pupil had been contracted, and there had been incomplete left hemiplegia. There were no symptoms of gastric trouble. The autopsy revealed a large tumor of the stomach to the left of the cardiac orifice; several smaller tumors in the right lung; a large tumor involving a portion of the scapula; and two tumors in the brain, one in the frontal lobe, $1\frac{1}{4}$ inches in diameter, and one in the posterior part of the parietal lobe, $\frac{1}{2}$ inch in diameter.

The second specimen was from a woman, forty-five years of age, in Dr. Northrup's service at the Presbyterian Hospital. Six months previously she had fallen and had convulsions, followed by some difficulty of speech and complete loss of power in the left arm and leg. She had recovered speech, and the paralysis had improved. About two days before her death there had been some rigidity of the neck. She had then passed into coma. At the autopsy, a tumor was found in the right parietal lobe, just behind the fissure of Rolando. It measured two inches in diameter, and involved the cortex, but did not reach the ventricle. It con-

tained viscid material. In the lung was a tumor, about half an inch in diameter. No other tumors were found. From its alveolar structure, the fact that the alveoli contained much mucin, that they were lined with cylindrical epithelium, that the tumor did not communicate with the ventricles, that it was apparently not connected with the membranes of the brain, and that there was a small tumor in the lung, he felt justified in concluding that this tumor was secondary to the nodule in the lung.

The third specimen was from a girl, sixteen years of age, who entered Dr. Ball's service at St. Luke's Hospital, complaining of vomiting and headache. She suffered from these attacks for two months or more before death. There were no other prominent cerebral symptoms, and she was supposed to be suffering from gastritis and hysteria. The vomiting occurred several times a day, and did not appear to depend upon the taking of food. About seven hours before death she complained of extremely severe pain in the head, and she was more than usually irritable and noisy. Then there was a general rigidity, lasting about an hour, and finally, general tonic convulsions with cyanosis. At the autopsy, along the upper and inner edge of the right temporal lobe and along the floor of the descending horn of the lateral ventricle, and invading the brain tissues in the immediate neighborhood, was a new growth, measuring 2 by 1 by 1 inch. Its consistency was like that of the brain. It involved the right optic thalamus and corpora quadrigemina. There were no other tumors. The growth consisted of very regular cylindrical cells covering the papillæ. From the fact that there was no other tumor, from its distinctly papillary character, the regular cylindrical cells, and from its situation at the border of one of the ventricles, the conclusion seemed inevitable that this was a primary papilloma of the choroid plexus, and the descending horn of the lateral ventricle.

The fourth specimen was from a man, forty-five years of age, who came into Dr. Thompson's service at the Presbyterian Hospital about eight months before his death. He

stated that four months before admission he had begun to suffer from lumbar pain, and three months later, from prickling and numbness in the legs and thighs, quickly followed by weakness. Then a marked "girdle" sensation had been felt about the waist. Over the trunk and legs was a marked reduction to sensibility, pain and temperature. During the last month of life he became very dull. The autopsy showed a tumor encircling the cord, and invading the eighth and ninth dorsal segments, and destroying all of the cord at that level except a little anteriorly. There was a small nodule in the lung, and in the brain were eleven tumors, varying from half to one and a half inches in diameter. These tumors were very vascular and papillary, the papillæ being covered with cylindrical epithelium. The tumor in the spinal cord had given rise to the clinical picture observed. It was conceivable that these numerous tumors in the brain and the one in the spinal cord might have been secondary to the tumor in the lung, which was about three fourths of an inch in diameter. Clinically it would appear that the tumor of the spinal cord was not the primary one, yet in the four cases reported it had been shown that a considerable neoplasm might exist in the brain without clinical symptoms. From the fact that the largest tumor in the body was in the brain, and was in the descending horn of the lateral ventricle, where two or three tumors had been recorded, and from the vascularity and papillary character of the tumors, he thought it was safe to conclude that the tumor began as a papilloma of the choroid plexus of the descending horn of the lateral ventricle, and afterwards passed into the category of carcinomata.

Dr. A. JACOBI asked why Dr. Thacher had suspected in the case of the adeno-carcinoma of the scapula that there was also a tumor of the alimentary canal.

Dr. THACHER replied that the regularity of the cylindrical cells and the mucous contents of the alveoli were probably the most striking features which had led him to think there might be a tumor in the alimentary canal.

The PRESIDENT said that he thought a metastatic tumor often preserved a suggestion of the structure from which it had developed. He had noticed this particularly in adenomata of the breast and of the stomach. In the former there was very frequently a distinct suggestion of a compound tubular gland preserved, although the growth might be extremely irregular in other respects and abundant. In the stomach he had noticed a preservation of the type of a simple cryptic gland.

Dr. WOOD exhibited under the microscope sections from a

TUMOR OF THE CEREBELLUM.

These sections had been taken from a patient who had been admitted to Dr. Kinnicutt's service at St. Luke's Hospital about two weeks before death. There had been cough and pain in the left side before admission, and on entering the hospital, bloody fluid had been found in the pleura, from which nearly a pure culture of tubercle bacilli had been obtained. About one week later the man had become comatose, and this had been associated with rigidity of the muscles of the arm, and some hyperæsthesia. At the autopsy, the pleura was found to be very much thickened, there were a few old cicatrices in the lungs, and a number of pale yellowish nodules scattered through the brain—two or three in the cerebellum, two or three in the cerebrum, and one in the optic thalamus. There was no new growth in the alimentary canal. The tumor of the cerebellum was thought to be an endothelioma, (1) because the cells were developed in the perivascular lymph spaces, and (2) because the growth had a distinctly tubular character.

Dr. THACHER said that at the autopsy he had felt positive that these were masses of tubercle, but the structure seen under the microscope certainly resembled carcinoma. As only one nodule had been examined microscopically he could not say whether the growth was endothelial or epithelial.

The Society then went into executive session.

Stated Meeting, February 26, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

LESIONS OF THE HEART AND BLOOD VESSELS.

Dr. GEORGE P. BIGGS presented four specimens illustrating sudden death due to

OCCLUSION OF THE CORONARY ARTERIES.

The first one was from a man, twenty-five years of age, a cooper by occupation. Alcoholism and syphilis were denied. The patient, after going up a flight of stairs, walked into a friend's room and sat down. After talking for a few minutes, his head suddenly fell upon his chest, the breathing became rapid, and the face cyanotic. He was speechless and could not be aroused. The ambulance arrived about fifteen minutes later, and then the breathing was slow, irregular, and shallow, and there was no perceptible radial pulse. On admission to the hospital, his breathing was shallow and irregular, he was cyanotic, and the pulse could not be felt. After free stimulation he revived sufficiently to answer a few questions. He stated that he had not been drinking for a year past, that he had no pain, and that he was extremely thirsty. In spite of the cyanosis there was no feeling of suffocation. He soon relapsed into unconsciousness, and œdema of the lungs developed very rapidly. He died about an hour and a half after the development of the first symptoms. At the autopsy, rigor mortis was well marked; there was no œdema; the diaphragm was at the level of the fifth space on the right side, and the sixth space on the left. The heart was found very greatly distended with blood, which was dark in color and largely fluid. The cavities of the heart were dilated and the walls correspondingly thin. The heart muscle was rather soft, but of normal color. The valves were normal except for slight thickening at the bases of the mitral and aortic cusps. There were several elevated, yellowish areas of atheroma in the aorta, 2 to 5 mm. in

diameter. Attached to two of these areas in the anterior portion of the aorta, just above the aortic valve, were two thrombi. The larger one of these was attached near the opening of the left coronary artery by three small finger-like projections only, and was irregularly cylindrical in shape, measuring 1½ by 1½ cm. It was found lying in the most anterior sinus of Valsalva, completely filling it and causing the aortic cusp, back of which it lay, to remain in the closed position. More careful examination revealed that the left coronary artery, which arose from this sinus of Valsalva, was completely closed over by the thrombus. The second thrombus was half a centimetre in diameter, and was attached loosely a little above the first one. The coronary arteries were moderately atheromatous. The kidneys showed slight chronic diffuse nephritis.

The speaker said that the case was interesting as showing how easily the cause of death in such a case might be overlooked. The smaller thrombus had fallen off notwithstanding the care taken in the removal of the heart, and was found only after careful search of the blood left in the pericardial sac. The larger thrombus, the one obstructing the coronary artery, was so loosely attached that it dropped off during the incision of the heart, and if the aorta had not been inspected from above before making the incision the position of the thrombus would have been entirely overlooked. Apparently the thrombi had been in existence for a considerable time, but had caused no trouble, as they had been regularly washed upward by the blood current. For some reason, the larger one suddenly fell backward, and occluded the left coronary artery, thus causing the sudden cardiac failure.

The second specimen was from an autopsy made some time ago for Dr. Robert Milbank. The patient, was a man of thirty-one years, who gave no history of syphilis, rheumatism, or malaria, and had enjoyed good health with the exception of attacks of what were described as "painful dyspepsia." He had recently taken a good deal of violent exercise. At

2 P.M. on the day of his death he had taken a hearty lunch with a friend at a club, and at 4 P.M. had been seized with severe epigastric pain. When seen by Dr. Milbank, he was suffering intensely, and was only temporarily relieved by the hypodermic injection of large doses of morphia. After an hour or two some watery mucus was vomited. The pulse was small and rapid, 110 to 124. The patient was conscious almost to the last, and walked across the room shortly before death. He died about six hours after the first symptoms. The autopsy revealed an embolus of considerable size, lodged in the left coronary artery. In the aorta were two small thrombi, one attached just at the mouth of the left coronary artery, the other attached a little higher up. A considerable portion of the thrombus at the mouth of the left coronary artery was missing, and was undoubtedly the source of the embolus in that vessel. There were no thrombi in the heart cavities. The organ was of normal size, and its valves were normal. There was an endarteritis of the aorta, apparently rather acute in character. The subpericardial adipose tissue was rather thick, particularly over the right ventricle. The other organs of the body showed no important lesions.

The third specimen was from a sailor, forty-eight years of age. Two days before admission to the hospital, while lifting a heavy weight, he had been suddenly seized with severe pain referred to the left hypochondriac region. This was soon followed by dyspnœa, and both pain and dyspnœa had been constant since that time. The pulse was found to be very irregular and feeble, the face extremely congested, and the feet were slightly œdematous. No cardiac murmur was audible. The respirations were rapid and feeble, and moist râles were heard over both sides of the chest, anteriorly and posteriorly. His temperature was 101.4°, respiration 56, and pulse 100. Notwithstanding free stimulation, he died a few hours after admission, and two days after the onset of the symptoms. At the autopsy the body was found to be very obese; rigor mortis was very marked; the diaphragm was at the sixth rib on the right side, and the sixth space on

the left side. Each pleural cavity contained 600 cc. of serous fluid, and the pericardium, 75 cc. of serous fluid. The heart was very greatly enlarged, its cavities were all very much dilated and distended with partially clotted blood. There was slight hypertrophy of the left ventricle. The valves of the left side were very slightly thickened, but no incompetence could be detected. An ante-mortem thrombus completely filled the left auricular appendix, and a second thrombus, measuring 2 by 1 ctm., was attached in the apex of the left ventricle. The most anterior sinus of Valsalva was completely filled with an ante-mortem thrombus, which held the cusp completely closed. This thrombus covered over the opening of the left coronary artery, and was continuous with a similar clot which filled the coronary artery almost completely for 3 ctm. The primary site of the development of this thrombus was apparently in the aorta very near the opening of the coronary artery. The aorta and coronary arteries were moderately atheromatous. The muscular substance of the heart was soft, pale, and friable throughout. The lungs were extremely œdematous. The spleen was normal. The kidneys showed a moderate amount of chronic diffuse nephritis. The right one contained a recent infarcation, one centimetre in diameter. The vessels at the base of the brain were moderately atheromatous. The other organs were practically normal.

The speaker said that it was probable that the dyspnœa and feeble, irregular heart action which suddenly developed shortly before death were due to a more complete closure of the left coronary artery. This obstruction was probably developed rather slowly, so that the disturbance of the heart action was not as marked as in the other cases.

RUPTURE OF THE HEART WITH MYOMALACIA.

For the fourth specimen, Dr. BIGGS said he was indebted to Deputy Coroner O'Hanlon, who performed the autopsy. It had been removed from a man of sixty years, who, for a

year or more, had been troubled with indefinite precordial oppression, and occasional attacks of angina. On the day of his death he went out, feeling as well as usual, but was suddenly seized with a severe attack of angina, just as he reached his destination. He succeeded in mounting a flight of stairs, but died almost instantly after doing so. At the autopsy the pericardial sac was found distended with blood. The heart was of normal size, and was covered with considerable adipose tissue. Just at the junction of the outer wall of the left ventricle with the interventricular septum was a large, ragged tear, about 2 ctm. in length. The cardiac muscle around this area was softened and torn. From this point of rupture the course of the blood was traced almost directly outward to the visceral layer of the pericardium. It then dissected its way upwards to the base of the ventricle, lifting up the pericardium and forming a large hæmatoma over the entire base of the left ventricle. The final rupture was shown by a linear, ragged tear of the pericardium, about 2 ctm. long. The valves and the coronary arteries were very atheromatous. About one centimetre from the origin of the right coronary artery the lumen of the vessel was very materially encroached upon by atheromatous deposit, and finally completely occluded by a recent thrombus. The rupture occurred in the particular area supplied by this artery, and was the result of myomalacia following its obstruction. Dr. Biggs referred to a recent article in the *Journal of Experimental Medicine*, in which Porter described some experiments he had made on dogs by ligating or partially occluding the coronary vessels. This experimenter's conclusions in part were: (1) That the frequency of the arrest of the heart as a result of this occlusion depended upon the size of the vessel ligated; (2) that the rapid closure of a coronary artery was invariably followed by death of the part it supplied, and that the process was a typical coagulation necrosis; and (3) the disturbed action of the heart and final arrest he attributed to the disturbance of the coördination of the heart, due to the anæmia of a considerable portion of

the heart muscle. On the passage of a glass tube down through the innominate into the coronary artery he noted invariably an almost immediate development of irregular heart action with a weakening of the contraction and lowering of the arterial pressure. If this occlusion were allowed to continue, the heart very soon became arrested. If the glass tube were soon removed, the symptoms disappeared and the heart's action returned to its normal state, showing that it was the anæmia of the part supplied which had disturbed the mechanism. By connecting the end of the glass tube with a supply of defibrinated blood diluted with salt solution, and supplying in this way nutrition to the area thus obstructed, he was able to keep up the normal action of the heart for a long time, thus demonstrating that the presence of the foreign body was not itself responsible for these symptoms. Cases of complete coronary obstruction, the speaker said, were rarely observed clinically, and still more rarely diagnosticated, owing partly to the suddenness of death and the variability of the symptoms. The clinical picture usually presented is briefly as follows: Rapid, irregular, feeble heart; dyspnœa and pulmonary œdema, with or without præcordial pain. The absence of pain was a characteristic feature of the first case presented, while in the second case the pain was described as "intense," and in the third and fourth cases as "severe." An interesting feature of the first two cases was the comparatively early age, twenty-five and thirty-one years, a period of life when coronary lesions are not usually expected.

The next specimen exhibited was one showing extensive replacement of the muscular tissue of the left ventricle by fibrous tissue. This was due to a gradual occlusion of the left coronary artery by atheromatous and calcareous changes. As the specimen had been previously presented to the Society, it was shown only as an illustration of the possible remote effect of coronary obstruction.

The last specimen in this series was one from a case of

ULCERATIVE ENDOCARDITIS.

The specimen had been removed from a male, thirty-seven years of age, who had been well up to nine days before his admission to the New York Hospital, when he had had a chill. On the second day of his illness he was feverish, and suffered from shortness of breath and pain in the left side. He then developed also cough with mucous expectoration. A second chill occurred on the sixth day. On admission, his temperature was 104°, respiration 40, and pulse 120. Physical examination showed an area of dulness with bronchial voice and breathing on the left side opposite the angle of the scapula, and near the spinal column. The heart action was regular, rapid, and strong. The urine contained a trace of albumen with granular casts. The patient improved under stimulation and tonic treatment up to the twenty-first day of his illness, when the temperature suddenly rose to 105.3°. For some days previously it had been below 100°, and his pulse had been between 72 and 80. The temperature was lower for four days, when another chill occurred, with temperature of 104.2°, followed by profuse perspiration. The blood was examined for malarial plasmodium, but none was found. After this time chills were of frequent occurrence, and were associated with profuse perspiration and a septic type of fever, the temperature frequently rising to 106° or 107°, and often falling to normal. Prostration rapidly increased, and he died during the tenth week of his illness, and in the sixth week after the development of symptoms of general sepsis. The autopsy revealed abundant adhesions over the left lung, and a few over the right lung. The heart was about normal in size; its cavities were dilated and greatly distended with blood; the muscular substance was pale and soft; the mitral and pulmonary valves were normal. Two of the aortic cusps were normal, while the third had attached to the lower two thirds of its inferior surface a large amount of grayish coagula. Three ragged perforations, the largest 4 mm. in diameter, were found through this aortic cusp in the area with which the thrombi were connected. Examination

of the cusps from above showed no vegetations, but there was conclusive evidence of the development of a large aneurism of the valve prior to the rupture. The tricuspid orifice was almost completely filled with firm, whitish thrombi, which were attached to the superior surface of the valve. The largest thrombus measured 2½ ctm. in diameter. All the thrombi were solid throughout. Examination in the fresh state and by cultures showed large numbers of capsule diplococci. A large part of the lower lobe of the left lung was still consolidated. There were a few areas of infarction in the upper lobe, and thrombi were present in many of the pulmonary vessels. The right lung contained infarctions, and the vessels leading to these areas were occluded by thrombi. The spleen was slightly enlarged and soft, but contained no infarctions. Both kidneys showed moderate parenchymatous degeneration; the right one contained an infarction.

The PRESIDENT, said that only a short time ago he had seen a review of a German article in which experiments like those described had been tried on dogs and rabbits. In this article, it had been asserted that total occlusion of the coronary arteries caused complete arrest of the heart in about two minutes, and that if the occlusion were complete for a short time only and the blood then readmitted to the vessels, the heart would recover. The specimen of interstitial myocarditis was of extreme interest in connection with the subject of aneurism of the heart.

Dr. HERBERT U. WILLIAMS, of Buffalo, presented a specimen of

AORTA WITH DISSECTING ANEURISM.

The patient, a man of fifty-eight years, had been under the care of Dr. Charles G. Stockton, who had first seen him on September 27, 1894. The patient said he had never been sick up to eight years before, when he had had a severe attack of pneumonia. The previous winter he had had some shortness of breath and tumultuous heart action, and

since then more or less dyspnœa on exercise or excitement. His height was five feet five inches, and his weight, 216 pounds. He presented a distinctly livid appearance; the pulse was weak and irregular; the capillary circulation was poor; there were dry cough and scanty mucous expectoration. Physical examination showed emphysema of both lungs with congestion at the bases. There was a systolic bruit at the apex of the heart, conveyed far to the left. The impulse was diffused and scarcely perceptible. When lying down, the patient's face became greatly congested. One month before this time this man had successfully passed an examination for life insurance. It was found that he voided 1824 cc. of urine in the twenty-four hours, which contained 17.8 grm. of urea; that the specific gravity of the urine was 1010, and that it was free from sugar and indican. Under treatment with digitalis, hot-air baths, and faradization, his general condition improved considerably. One morning he was found dead in bed without having made any complaint during the night. The autopsy was made about twelve hours after death. Rigor mortis was firm. The subcutaneous fat was three fourths of an inch thick over the thorax and two inches over the abdomen. There was a quantity of bloody serum in the left pleural cavity, and a large firm blood-clot. The right pleural cavity was empty. The heart was very large, its muscle thick and firm, and there was hypertrophy and dilatation, especially of the left ventricle. The mitral orifice admitted two fingers. The valves were stretched, but not thickened. There was moderate atheroma of the ascending aorta. The left kidney was large, firm, and contained several small cysts. The capsule was somewhat adherent, and the surface beneath granular. The right kidney presented a similar condition. The kidneys showed under the microscope the changes of chronic diffuse nephritis. The spleen and liver were normal; the stomach small, and the large intestine and vermiform appendix were normal. The upper and posterior wall of the aorta, close to the left subclavian artery, exhibited an opening,

one fourth of an inch in diameter, and nearly round. It was supposed at first to communicate with the descending aorta, which had ruptured into the pleural cavity. An aneurismal dissection in the thoracic aorta appeared to the left and in front, extending behind beyond the middle line to the right. Between the tenth and eleventh intercostal arteries it was far over to the right and behind. At the level of the renal arteries it had travelled still farther around, and a little below this point it entirely encircled the pair of aortic trunks to be subsequently described. It reached to the bifurcation of the aorta, and on the right common iliac to its bifurcation into the external and internal iliacs. The opening below the left subclavian artery did not communicate directly with the aneurism, but with a vessel which was continuous with the left common iliac. What was supposed to be the main aorta was continuous with the right common iliac. The dissecting aneurism surrounded both vessels more or less completely. The aneurism had its origin in a rupture, not of the main aorta, but in the channel to the left of it. It had stripped off the pleura on the left side, and had broken through this, causing the fatal hemorrhage into that cavity.

A careful examination showed that there was a duplication of the aorta from the left subclavian down, the two portions being separated by a complete septum. The right was the larger, and was in line with the descending limb of the arch. The left branch did not exhibit arterio-sclerosis. The principal vessels arose from the right branch except the inferior mesenteric, which was given off from the left and behind. The cœliac axis, superior mesenteric, and both renal arteries arose from the right or principal branch. There were ten pairs of intercostal arteries arranged along the right vessel, most of them patulous. Many of the intercostals opened from the right vessel into the left, and went no farther.

The interpretation of the condition was not perfectly clear. Whether the second aortic vessel could be accounted for as

a defect of development, or as having originated through some pathological change, might be decided after opening both vessels completely, so as to determine all their relations. That had been deferred to permit of the exhibition of the specimen unaltered.*

Dr. JAMES EWING presented a specimen of

RUPTURE OF THE AORTA,

removed from a woman, twenty-six years of age. She presented no personal or family history of importance. The illness had begun three years before death with the ordinary symptoms of acute nephritis developing after exposure to cold. It was characterized at the onset by œdema and dyspnœa. These symptoms continued irregularly for about one year, after which uræmic symptoms were added. She entered the hospital on January 27th, and was then pale and cyanosed. There was a paralysis of the right side of the face, which had appeared three months before. The pulse was 100, somewhat irregular, and showed remarkably high tension. There was severe and constant headache, and a constant feeling of sinking and choking about the heart. She was given the usual remedies for reducing arterial tension without much effect, and they were finally stopped. Within two hours after discontinuing the use of arterial dilators, she complained of severe pain in the chest, and became greatly prostrated. The house physician then found in addition to the loud systolic murmur, heard all over the precordium, a remarkably harsh double murmur, heard loudest over the aortic valve. The patient went into collapse, and died within an hour. At the autopsy, the kidneys were found to be of about the normal size, the surface was coarsely granular, the capsules non-adherent, the

* Subsequently when the two vessels were opened, it was found that the right vessel bifurcated into two common iliacs, though a probe inserted from above had passed into the right common iliac alone. The left vessel followed the course of the left of these two common iliacs and divided into two portions corresponding to the external and internal iliacs, into which they opened respectively, after a short course along their walls.

cortex irregular in thickness, the markings obliterated, and the kidney tissue in part replaced by uric acid infarcts. There was very little congestion of the kidney. The heart was moderately enlarged. The wall of the left ventricle was very considerably hypertrophied without dilatation. There was no roughening of any of the valves, and there was only very slight atheroma. On opening the pericardium, a large amount of fresh bloody serum was evacuated. The heart was surrounded by a thick dark clot. Some difficulty was experienced in finding the origin of the blood, so the abdominal viscera were removed, and the aorta stripped up. On reaching the aortic valve, the finger was passed into a peculiar pouch. About one inch above the aortic cusps was a clean, linear rupture of the whole aortic wall, and through this rupture the blood had infiltrated the tissues around the aorta, and rupturing into the pericardium had infiltrated the tissues of the aorta to the middle of the transverse arch. At the origin of the left subclavian artery could be seen a healed partial rupture of the subclavian vein, about three quarters of an inch in length, which appeared as if the intima and media had been slightly displaced on the adventitia. The remainder of the aorta showed very little atheroma.

The speaker remarked that at least two such cases had been reported to the Society within the past few years.

Dr GEORGE P. BIGGS said that about a year and a half ago Dr. Ferguson had presented to the Society a specimen showing a vertical linear rupture in the aorta, situated just a short distance above the aortic valve. In this case the blood, after having dissected along the aorta nearly its entire length, had finally broken through into the pericardium, causing sudden death.

Dr. VAN HORNE NORRIE recalled a case of rupture of the aorta, seen about two years ago in a male patient in St. Luke's Hospital. This man was suffering from phthisis, and nothing unusual had been noticed until about half an hour before his death, when, after a sudden attack of pain

around the heart, he went into collapse and died. The autopsy showed complete transverse rupture of the aorta about one inch above the aortic orifice, and a large amount of blood in the pericardial sac. The gross appearance of the aorta was normal.

Dr. EWING said that Dr. Delafield thought that the primary cause of the rupture in the case he had just reported had been the high tension of the arteries and over-action of the heart. From the gross and microscopical appearances of the specimen presented, it was evident that the rupture had not been due to the giving way of a cicatrix of syphilitic origin.

The Society then adjourned.

Stated Meeting, March 11, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

Dr. EUGENE HODENPYL presented a series of specimens illustrative of

THE ASSOCIATION OF MALIGNANT DISEASE AND TUBERCULOSIS.

For the first specimen he was indebted to Dr. Thacher. It had been removed from a man, fifty-three years of age, who ten months ago had developed a small tumor on the right side of the neck, opposite the thyroid cartilage. One month later, the growth had been removed at the German Hospital. It had soon reappeared. When next seen, it extended up from behind the angle of the jaw to the median line, was nodular, very hard, and adherent to the skin, jaw, and deep structures. There was some superficial ulceration. One week ago the breathing became very difficult and painful. The urine was normal. The temperature varied from 99.5° to 101.5°. At the autopsy the upper lobes of the lungs were found to be the seat of a recent tuberculosis,

and the tongue contained an epithelioma. On the right side, opposite the thyroid cartilage, was an infiltrating growth, which had ruptured into the œsophagus. Several sections had been examined, but no evidence of tuberculosis found in the epitheliomatous mass.

The second specimen showed not only the two lesions occurring in the same individual, but the combination of the two diseases in the same lymph nodes. The patient, a man of forty-four years, gave no tuberculous or syphilitic history. He had had a small gland in the neck since childhood, but it had not undergone any appreciable change during all this time. Last March a small ulcer was noticed on the right side of the tongue, which soon healed. During the summer, a small, painless lump appeared under the jaw. Last November an ulcer appeared on the tongue, and soon began to increase rapidly. On admission, in February, he was moderately emaciated, and was expectorating profusely. On the right side of the tongue and floor of the mouth was a small growth, which was somewhat ulcerated. There was an enlarged lymph node underneath the angle of the jaw. Dr. McBurney removed the tongue by Kocher's operation, together with the lymph node. In the lymph node (shown under the microscope) was a combination of the lesions of tuberculosis and epithelioma. He had stained a number of sections for tubercle bacilli, but with negative result. The miliary tubercles were slightly cheesy in their centres, and contained a considerable number of giant cells.

The speaker said that George Clement, in *Virchow's Archives* for 1895, had presented an excellent *résumé* of the literature of the subject. The combination of tuberculosis and epithelioma or carcinoma in the same organ had been described by a number of observers, but in all, less than fifty typical cases of this kind were on record. The combination of tuberculosis and epithelioma in the same individual was much more frequent. Lubarsch's conclusions, from his study of the subject, are: (1) That carcinoma may be engrafted on an old tuberculosis, and that half of all the cases reported

belong to this class; (2) that an old case of tuberculosis may become carcinomatous, and the carcinomatous cachexia facilitate a fresh tuberculous eruption—a rare occurrence; (3) that a carcinomatous person may become tuberculous, although only three instances of this kind were found on record; (4) that a chronic, progressive tuberculosis may act as a predisposing cause to carcinoma in the same manner that a local traumatism predisposes to malignant disease. Dr. Hodenpyl said that in the case reported, it seemed to him that the two lesions were probably nearly simultaneous in their occurrence. There was no tuberculosis found in the primary tumor.

Dr. GEORGE P. BIGGS said that this specimen was interesting to him in connection with the case of giant cells which he had presented some time ago; the two conditions might easily be confounded. The rarity of the association of malignant disease and tuberculosis seemed to him to be partly explained by the different periods of life in which these diseases ordinarily developed. One susceptible to tuberculosis usually succumbed to this disease before arriving at the age at which carcinoma or epithelioma ordinarily developed.

Dr. J. S. THACHER recalled a case seen clinically about one year ago occurring in a nurse about forty-five years of age. This woman had presented only certain vague abdominal symptoms, and several physicians had failed to make a positive diagnosis. At the autopsy there was some difference of opinion as to whether the case was one of tuberculosis or carcinoma. The peritoneum seemed to show typical miliary tubercles, but in the pancreas were nodules looking more like carcinoma. Dr. Coleman found, on making sections, that both conditions were present, the tuberculosis involving principally the peritoneum.

The PRESIDENT said he thought he had discovered in the specimen under the microscope areas of cheesy degeneration in the newly formed epitheliomatous tissue, suggesting that at east in those places the tuberculosis was of more recent

development than the epithelioma. He could not see any reason why tuberculosis and carcinoma should not be associated; it was a pure assumption to suppose that they were in any way antagonistic. He recalled a case of extensive secondary carcinoma and diffuse pulmonary phthisis in the same lung. He thought such cases were not so very rare; probably they had been overlooked, or were not thought worth reporting.

Dr. HODENPYL then presented microscopical specimens of

MULTIPLE MILIARY ANEURISMS OF THE LEFT ANTERIOR CEREBRAL ARTERY.

These had been taken from a rather elderly lady who, while apparently in fair health, had suddenly fallen forward from her chair, and become unconscious. She died soon after admission to the hospital. At the autopsy, the thoracic and abdominal organs were found comparatively normal. There was no atheroma of the larger vessels of the thorax and abdomen. There was, however, a well marked atheroma of all the vessels at the base of the brain, and the left anterior cerebral artery presented what looked to be multiple miliary aneurisms. The vessel was studded with from ten to fifteen small nodules, varying in size from that of a pin's head to three or four times that size. There was a considerable extravasation of blood at the base of the brain; evidently the hemorrhage had occurred from rupture of one of these small nodules. Microscopical examination showed very extensive disease of the vessels. In at least one place, rupture had taken place into a blood vessel, so that it was really an aneurism; in the other places, the more accurate designation would be "atheromatous cysts."

ACUTE EXUDATIVE MENINGITIS.

Dr. HODENPYL then presented microscopical specimens from a case of this condition in which there had been scarcely any gross lesions. He thought the diagnosis could not have

been made except by the aid of the microscope. The patient, a colored man, twenty-three years of age, was admitted to the hospital on January 19, 1896. He was very intemperate in his habits, and had had syphilis two years before. About the middle of last November, he had begun to suffer from dizziness and headache, but these symptoms had temporarily improved under anti-syphilitic treatment. The headache had then returned and become more severe. On admission, he was well nourished ; the breath was foul ; there was considerable prostration ; the urine was normal ; the temperature was 100, pulse 66, and respiration 22. The physical examination was negative. On the day after admission he was found to be stupid, and he passed no urine. Fourteen ounces of urine were drawn by catheter. On January 22d, two days later, there were convulsions and coma. The next day he could hardly be aroused from his stupor. On January 25th there were convulsions again. On January 28th he died. While in the hospital the temperature had been between 99° and 100.8°, the pulse between 64 and 128, and the respiration between 16 and 24. At the autopsy, the pia mater was congested, and somewhat dry, and although its lustre was slightly diminished, its appearance was not at all characteristic. A very small amount of clotted blood was found at the base of the brain, and a little slightly blood-tinged fluid in the lateral ventricles. All over the convexity of the brain on either side, the microscope showed a moderate exudation in the meshes of the pia, and little on the surface. The exudate consisted of serum, fibrin, and leucocytes, with a few blood cells and cells from the pia itself.

The speaker said that three kinds of meningitis normally showed no gross lesions, viz. : (1) Acute cellular meningitis, which was comparatively rare ; (2) tuberculous meningitis, either with or without exudative meningitis ; and (3) acute exudative meningitis. It seemed to him quite remarkable that such a small lesion should prove fatal, as it undoubtedly did.

Dr. GEORGE P. BIGGS referred to a similar case, that of a

girl who had frequently been in the Hudson Street Hospital for hysteria. One day, just as she was about to be discharged from the hospital, she fell dead. The autopsy showed no very clear cause of death, except that the pia mater seemed to be a little dry and dull. Microscopical examination was made of the medulla, cerebellum and cerebrum, and in all these parts an exudate was found. This consisted of an extremely thin layer, but containing many cells. The rapidity with which death might occur in these cases was interesting. He remembered a case in which a boy had died within twenty-four hours of the onset of the first symptoms. Microscopical examination in this case disclosed the cause of death.

The next specimen presented by Dr. HODENPYL was from a case of

PRIMARY CARCINOMA OF THE LIVER AND HEAD OF THE PANCREAS.

It had been taken from a woman, twenty-seven years of age, who had been comparatively well up to one year before her death. At that time she had begun to have some jaundice and offensive diarrhœa, with abdominal pain. For three weeks prior to admission she had had pretty constant pain to the right of the epigastrium. On admission, she was moderately emaciated, intensely jaundiced, and suffering considerable pain in the epigastrium. The abdomen was moderately distended with fluid. The area of liver dulness was very decidedly increased, and also the splenic dulness. There was an irregular fever, the temperature sometimes rising as high as 103°. About two days before death an exploratory operation was performed. An enormously distended gall-bladder was found, and also a new growth in the region of the pancreas. An anastomosis was made between the gall-bladder and the intestine by means of a Murphy button. Death occurred from peritonitis and shock. At the autopsy the abdomen was found to contain about two

quarts of bloody fluid, and the intestines were distended with tarry blood. The intestinal suture was tested and found to be complete. The gall-bladder contained two ounces of dark bile. The stomach was dilated, and the mucous membrane bile-stained. The left half of the pancreas was soft. The organ was greatly enlarged, and behind and firmly adherent to the duodenum and under surface of the liver was a new growth. In the duodenum were two circular openings with rounded edges, communicating directly with the necrotic new growth. A probe passed only a short distance into the common duct. The gall-bladder at the cystic duct opened by a solution of continuity directly into the cancerous mass. The liver was enlarged and intensely bile stained. The gall-ducts were greatly congested. The kidneys showed acute degeneration.

The PRESIDENT remarked that some time ago he had dresented similar cases to the Society. In two of them the patient had died so early that all that was found was a nodule restricted to the head of the pancreas. The particular interest in the case was the demonstration of the fact that carcinoma did occasionally begin in the head of the pancreas.

CARCINOMA OF THE LIVER AND STOMACH.

The next specimen presented by Dr. HODENPYL was from a man, fifty-two years of age, admitted to the hospital in November. He had been operated upon three months before successfully for hydrocele. At the time of his last admission, the abdomen was distended, but no fluid was withdrawn from it. Physical examination showed the liver considerably enlarged. Emaciation and enlargement of the liver were the only evidence of disease, and these were steadily progressive up to the time of his death. At the autopsy, there were three quarts of bloody fluid in the abdominal cavity. The liver weighed twelve pounds, and was almost completely replaced by carcinomatous new growth.

At the pylorus was a carcinomatous mass, just beginning to ulcerate. There was also a small carcinomatous mass at the head of the pancreas.

PRIMARY CARCINOMA OF THE STOMACH WITH PERFORATION THROUGH THE DUODENUM INTO THE LUNG.

The patient from whom Dr. HODENPYL took these specimens was a man, fifty-one years of age, who gave a history of vomiting after meals for a year before death. Shortly before death he developed some fever and cough, with very fetid expectoration. In the lesser curvature of the stomach the autopsy revealed a large carcinomatous mass, and an opening admitting two fingers. This opening passed into the lower lobe of the lung, in which was an abscess about the size of an orange.

The next specimen was one of

CARCINOMA OF THE PYLORUS,

removed from a man, fifty-six years of age, who had had vomiting and slight pain in the stomach for two years previously. He had emaciated gradually, but there had been no vomiting of blood. Microscopical examination showed the carcinoma to be of the colloid variety.

The next specimen was from a case of

CARCINOMA OF THE STOMACH WITHOUT SYMPTOMS.

It was removed from an old man who had been found in the street bleeding from the mouth. He died at the hospital before any history could be obtained. At the autopsy, the man looked to be strong and well nourished. The stomach and intestine were filled with large blood clot; the stomach contained a large coagulum, and at the cardiac orifice was an encircling and constricting carcinomatous mass with a number of blood vessels traversing this ulcerated growth.

The next specimen was one of

CARCINOMA OF THE STOMACH WITH MARKED CONSTRICTION OF THE PYLORUS,

without clinical history.

The last specimen by Dr. HODENPYL was one of

SYPHILITIC PERFORATION OF THE LARGE INTESTINE,

occurring in a man, sixty-one years of age. He had had a well marked attack of syphilis for which he had been treated. There was a syphilitic necrosis of the sternum. He came into the hospital complaining of obstinate constipation. Enemata and powerful purgatives were given without causing a movement of the bowel. At the autopsy several syphilitic gummata were found in the spleen, and in the abdominal cavity was a beginning peritonitis. There was also a large quantity of fæcal matter in the abdominal cavity.

A PEYER'S PATCH IN A MECKEL'S DIVERTICULUM.

Dr. THOMAS S. SOUTHWORTH presented the intestine of a child of seven months, who had died of chronic catarrhal entero-colitis. The solitary follicles were enlarged and Peyer's patches swollen. About one foot above the ileo-cæcal valve was found a small Meckel's diverticulum, in which was a Peyer's patch.

ILEO-COLIC INTUSSUSCEPTION.

The second specimen was from a child of two months, evidently syphilitic. There had been high fever and some pulmonary consolidation just before death. At the autopsy, the posterior portions of the two lower lobes showed patches of broncho-pneumonia. The spleen was enlarged, apparently from syphilis, and the organ weighed thirty grammes. In the lower portion of the ileum were six intussusceptions, and one of them of the typical ileo-colic variety. These intussusceptions, the speaker said, occurring just prior to death, are usually in the jejunum.

The Society then went into executive session.

Stated Meeting, March 25, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

Dr. GEORGE C. FREEBORN read a paper with this title:

"RÉSUMÉ OF THE USES OF FORMALIN."

This reagent is also known in commerce under the names of formol and formalose. It is a forty-per-cent. solution of the gaseous body, formic aldehyde (HCOH), in water. It is prepared by oxidizing methylic alcohol and bringing the resulting gas into solution in water. It is non-inflammable. It mixes in all proportions with alcohol and water. Its power of penetration is good. Its keeping properties are good. A series of experiments were instituted to determine this point, with the following results: A forty-per-cent. solution was kept in open and closed vessels, daily tests being made. The results of these experiments showed that the solutions did not decompose. There was a loss of 1.6 per cent. of formalin and an increase of 0.1 per cent. of formic acid. Polymerization took place with the formation of a butterlike mass containing sixty per cent. of formic aldehyde; this dried up into a hard mass which contained eighty-five per cent. of formic aldehyde. Fish and others advise that it be kept in darkened bottles, as the light may decompose it. In an experience of two years I have not noted any appreciable change in the solutions.

Attention was first called to the antiseptic properties of formalin by F. Blum, in 1893. In 1894 Pottevin found that when formalin was added to cultures of bacteria, their growth was arrested. Cohn also found that solutions and the vapor of formalin killed bacteria both in the vegetative and in the spore stage, but that it had but little action on molds unless used in strong solutions. This want of action on molds has also been noted by many other observers.

Miquel, in experimenting with gaseous form cialdehyde, found that it acted as a disinfectant for small and loose objects confined in small spaces, but was not reliable for disinfecting large rooms.

Cambier and Brochet also experimented with the gaseous form, with results similar to those of Miquel. Their laboratory experiments were satisfactory, but their attempt to disinfect a large room did not give perfect results. They, however, demonstrated the fact that layers of dust a centimetre thick were rendered sterile. They also devised a portable apparatus for producing the gas.

Alleger made quite an extensive series of experiments in order to determine the germicidal action of formalin on bacteria. He made use of cultures of the bacillus of diphtheria in Petri dishes. The surfaces of these dishes were sprayed with solutions of formalin varying in strength from 1 to 10,000 to 1 to 100. He found that a solution of 1 to 2,000 prevented the growth of the bacillus but not that of molds. Another series of experiments were made with stick cultures in test tubes. Five drops of solutions of formalin, varying in strength from 1 to 20,000 to 1 to 100, were placed on the surface of the culture media in each tube. At the end of forty-eight hours none of the tubes which had been treated with a 1-to-100 or stronger solution showed any growth. A third series of experiments were made with smear cultures, which were allowed to grow for from twenty-four to forty-eight hours and then they were treated with the above-mentioned solutions of formalin for a few minutes. Cultures were then made from these, with the result that no growth took place from those treated with the stronger solutions.

Formalin has also been used in surgery, obstetrics, and gynæcology as an antiseptic, but has had to be abandoned on account of its irritating properties.

As a preserving agent formalin was first used by the botanists. Cohn experimented with it extensively, and found that the green and red colors of plants were not ex-

tracted. At the end of five months his specimens still retained their natural colors and were not shrivelled. The botanists Sadebeck and Holfert recommend it highly.

It was first introduced into the zoölogical technique by F. Blum, who obtained excellent results with it as a preservative agent, and it has now come into general use.

The excellent results obtained by the botanists and zoölogists with formalin as a preservative soon resulted in its introduction into the anatomical and histological technique, and at the present time it is quite generally used.

As a preservative agent for gross specimens, it is used in the strength of two per cent.,* though weaker solutions, from three quarters to one per cent., have been used. These weaker solutions are objectionable on account of the likelihood of the growth of molds, and because they cause more or less swelling of the tissues. As the result of the experience of numerous observers, it appears that five-per-cent. solutions give better results.

The quantity of the solution should be large—a hundred times the volume of the specimen—and the fluid should be renewed at the end of twenty-four hours. In some cases it is well to renew the fluid a second or even a third time.

Formalin used in this manner preserves the natural form, the transparency, and, to a certain extent, the natural color of the specimens. In some specimens the blood-color appears to be bleached out, but if the preparation is placed in strong alcohol this is nearly if not entirely restored.

* Bolles Lee (*Anat. Anz.*, xi., 1895, p. 253) calls attention to what he considers an inaccurate use of the terms formol, formalin, and formaldehyde; also to the manner of stating the percentages used. He maintains that the proper way of stating the strength of the solutions is to say "formol or formalin diluted with so many volumes of water."

Parker and Floyd (*Anat. Anz.*, xi., 1896, p. 567) reply to the criticism made by Bolles Lee in the above-cited article. They contend "that for the sake of consistency the same method of expression ought to be used for alcohol—*i. e.*, ninety-five volumes of alcohol and five volumes of water. These expressions seem to us unnecessarily cumbersome, and as they are in no way more precise or less ambiguous to one familiar with the meaning of per cent. than the expressions we used, we prefer them."

For preserving the blood-color of specimens, Johres makes use of the following procedure and fluid:

Sodium chloride	1 part;
Magnesium sulphate	2 parts;
Sodium sulphate	2 "
Water	100 "

To this mixture are added from five to ten parts of a forty-per-cent. solution of formalin. After the specimen has become sufficiently hardened, pour off the formalin solution, wash the specimen in ninty-five-per-cent. alcohol, then keep it in ninety-five-per-cent. alcohol until the blood-color becomes restored, and finally preserve it in a mixture of equal parts of glycerin and water.

Fish makes objection to the use of formalin as a permanent preservative on account of the large amount of water present, which might cause freezing, and advises the addition of an equal volume of alcohol. Hodenpyl,* in using formalin for making sections on the freezing microtome (see below), found that the least trace of formalin left in the specimen prevents its freezing. It would therefore seem that Fish's objection is not valid.

Koehler and Lumière found that if from fifty to a hundred and fifty cubic centimetres of a solution of one volume of formalin diluted with four volumes of water were injected into the gastro-intestinal canal of small animals by the mouth and anus, also into the carotid artery, and the animal was kept hung up in the air, in a dry place, for some weeks, it was perfectly preserved without distortion. They performed an autopsy on an animal—a guinea-pig—treated in this manner, four months after, and found the tissues and organs perfectly preserved. Dr. Henry Power† has treated the bodies of children in a manner similar to this with good results.

Professor George S. Huntington informs me that he has

* Personal communication.

† *Ibid.*

used formalin for the preservation of organs. He injects a solution of from two to twenty-five per cent. into the blood-vessels. and the result is a perfect preservation of the form and color of the organ. He has found that it is of no use for preserving dissecting material.

For the preservation of brains formalin has given excellent results. The fresh brain is placed in a ten-per-cent. solution, and at the end of ten days it will have sufficiently hardened to permit of the making of thick sections for demonstration of the gross anatomy, the distinction between the white and gray matter being more sharply defined than when alcohol is used.

Parker and Floyd confirm the observations of Lanzilotti-Buonsanti, Hoyer, Hoffer, and others, in regard to the swelling of the brain when formalin alone is used. In a sheep's brain they found this swelling to be forty per cent. of its original volume. In order to correct this defect they experimented with various reagents in combination with formalin. They finally found that a mixture of six volumes of ninety-five-per-cent. alcohol and four volumes of a two-per-cent. solution of formalin gave nearly perfect results. Sheep's brains hardened in this mixture retained their original color and form, and were very little increased in volume. "A brain that before treatment (June 20th) measured one hundred and one cubic centimetres, when finally prepared (July 15th) measured one hundred and three cubic centimetres."

Fish states that an excellent hardening of the brain may be obtained with the following mixture:

Water	2000 c. c.;
Formalin	50 "
Sodium chloride	100 grms.;
Zinc chloride	15 "

The specific gravity should be about 1.05. The brain is left in this mixture for a week or ten days. The blood-

vessels and cavities should be injected with the fluid if possible. After the end of the ten days the brain is transferred to formalin, 50 cubic centimetres, and water, 2,000 cubic centimetres, where it may be kept indefinitely; or, after being a week in this fluid, it may be first transferred to fifty-per-cent., then to ninety per-cent., and finally to ninety-five-per cent. alcohol. He has also treated portions of the adult central nervous system by this method, and afterward with mercuric chloride, picro-aceto-sublimate, and chromacetic-acid mixtures, with good results.

For hardening eyes Leber used formalin mixed with water in the proportion of one to ten. The natural color and transparency of the organ were retained. The cornea and lens became but slightly cloudy. In his opinion, the fine structure was as well preserved as with Müller's fluid. If the eyes were placed in alcohol the cornea and lens became opaque. I have employed formalin in a five-per-cent. solution for this purpose with the same results.

As a hardening agent for microscopic work, formalin has been used very extensively, the strength of the solutions employed varying from one per cent. to the full strength—forty per cent. As the results of many observations, it may now be said, with possibly one or two exceptions, that formalin alone is an unfit reagent for hardening tissues for microscopic work. It was condemned by Hermann in 1893; Lachi states that it has an injurious effect on connective tissues, smooth and striated muscle, and embryos. Many other observers condemn its use without being so specific as Lachi.

The exceptions, where it gives satisfactory results, are mucous membranes and the central nervous system. I have used it in five-per-cent. solution for hardening cystic adenoma of the ovary, with good results; also for the mucous membrane of the uterus.

Lachi, who has condemned its use for all other tissues, speaks well of its action on the central nervous system.

Van Gieson has employed it in four-, six-, and ten-per-

cent. solutions for hardening the central nervous system. The ganglion and nerve fibres were well fixed. Sections stain well with Weigert's hæmatoxylin method. He has also used it for hardening the central nervous system for after-staining with Rehm's modification of Nissl's method. The results were good, but not quite so sharp as with alcoholic hardening.

The best results for microscopic work are obtained when formalin is combined with other fixing reagents. When it is used in combination with the chrome salts more rapid penetration is obtained, whereby the time required for hardening is shortened. I have used a solution of formalin in Müller's fluid made as follows:

Potassium dichromate	2 grammes;
Sodium sulphate	2.5 "
Two-per-cent. solution of formalin	100 c. c.

With this fluid I have obtained excellent preservation of the ovary, the uterus, etc. At the end of forty-eight hours the specimen is cut into slices an eighth of an inch thick; these are washed in water for two hours; they are then placed in alcohol for twelve hours, and then carried through the usual processes of imbedding in celloidin. Specimens hardened in this manner show no shrinkage, and the tissue elements are well preserved.

Landowsky recommends the following fixing fluids for mitotic figures in cells:

1. Water	20	c. c.;
Alcohol (ninety-five per cent.)	10	"
Formalin	3	"
Hydric acetate	0.5	"
2. Water	30	c. c.;
Alcohol (ninety-five per cent.)	15	"
Formalin	5	"
Hydric acetate	1	"

Probably the most successful use of formalin in histological technique is its substitution for osmic acid in the

osmium-dichromate fluid used in Golgi's silver method for the central nervous system.

This substitution was probably first made by Dr. O. S. Strong, though it has been recommended by Lachi and others. Strong employs the following mixture:

Potassium dichromate (3.5- to five-per-cent. solution)	100 vols.;
Formalin	2.5 to 5 vols.

After the specimen has been in the solution for several days it is transferred to a one-per-cent. silver-nitrate solution; or at the end of two days it is transferred from the formalin-dichromate mixture to the following:

Potassium dichromate (five-per-cent. sol.)	2 vols.;
Formalin	1 vol.

After remaining in this fluid for from twelve to twenty-four hours it is placed in the silver solution. The advantages of this method are, that the stage of hardening is prolonged, the stage favorable to impregnation lasts longer, and the results are more certain. For embryonic tissue he does not consider it as good as the osmic-dichromate mixture.

Fish has used the above-described method, but thinks he has obtained better results with the following:

Müller's fluid	100 c. c.;
Formalin (ten per cent.)	2 "
Osmic acid (one per cent.)	2 "

Strong has also used formalin as an injection medium for hardening brains *in situ*. He uses formalin diluted with an equal volume of water. This he injects into the cerebral vessels until it runs out of the cut jugulars. After a few minutes he makes a second injection, then a third, and even a fourth, at intervals of fifteen minutes. The brain is then removed from the cavity of the skull. The swelling which usually occurs when formalin is used does not take place.

Sections from brains hardened in this manner may be stained by either the Weigert or the Golgi method. When the Golgi method of staining only is to be used an equal volume of a ten-per-cent. solution of potassium dichromate is added to the formalin in place of the water.

Dr. T. S. Cullen has devised two methods for using formalin in connection with frozen sections. They are as follows:

Method I.

1. Keep sections made with the freezing microtome in a five-per-cent. aqueous solution of formalin for three to five minutes.
2. Keep them in fifty-per-cent. alcohol for one minute.
3. Keep them in absolute alcohol for one minute.
4. Wash them in water.
5. Stain them in hæmatoxylin for two minutes.
6. Decolorize them in acid alcohol (1.5 per cent. HCl).
7. Wash them in water.
8. Stain them with eosin for twenty seconds.
9. Place them in ninety-five-per-cent. alcohol.
10. Pass them through absolute alcohol, clear them in creosote or oil of cloves, and mount them in Canada balsam.

The blood being lost in the frozen sections, the defect was overcome by fixing the tissue in formalin, and then making frozen sections as in

Method II.

1. A piece of tissue $1 \times 2 \times 5$ centimetres is kept in a twenty-per-cent. aqueous solution of formalin for two hours.
2. Frozen sections are made.
3. Keep them in fifty-per-cent. alcohol for three minutes.
4. Keep them in absolute alcohol one minute.
5. Wash them in water and stain them in hæmatoxylin for two minutes.
6. Decolorize them in acid alcohol (1.5 per cent. HCl).

7. Wash them in water.
8. Stain them in eosin for twenty seconds.
9. Place them in ninety-five-per-cent. alcohol.
10. Pass them through absolute alcohol, clear them in creosote or oil of cloves, and mount them in Canada balsam.

Method I. is used for diagnosticating bits from tumors, and it is possible to make a report in fifteen minutes. Method II. is used mostly for the examination of uterine curettings. The author's practice is to have bottles containing a ten-per-cent. solution of formalin in the operating room. The curettings are immediately placed in one of these, and by the time they reach the pathologist they are hard enough to make frozen sections of.

Bender has also used formalin for making frozen sections, not for preliminary hardening, as in Cullen's method, but for completing the hardening of specimens that have already been in alcohol. He places pieces of tissues, two millimetres thick, that have been in alcohol, in a one-per-cent. solution of formalin, and keeps them there until the alcohol is completely removed. This requires from half an hour to an hour. He then washes them well in water and makes frozen sections. The tissue, he states, is rendered soap-like in consistence by the action of the formalin.

Ohlmacher states that formalin, when used in from two- to four-per-cent. solutions, acts as a powerful mordant for aniline dyes. Cover-glass preparations are treated for one minute with the solution, washed well in water, and then stained in the cold. Or it may be used instead of aniline oil or carbolic acid as a menstruum for dissolving the dyes. One gramme of fuchsine or other aniline dye is dissolved in ten cubic centimetres of alcohol, and this is added to one hundred cubic centimetres of a four-per-cent. solution of formalin. Formalin methylene blue, made by dissolving one gramme of methylene blue in one hundred cubic centimetres of a four-per-cent. solution of formalin, makes an effective stain. A saturated solution of safranin in a four-per-cent. solution of formalin gives a beautiful double stain

when used after the formalin methylene blue. Nuclei stain blue, plasma stains reddish.

S. H. Gage has used the following solution as a dissociating agent with good results:

Normal salt solution.....1000 c. c.;
Formalin (forty per cent.)..... 2 "

Formalin has been used by Hauser for preserving plate and tube cultures of bacteria. His method is as follows: Plate cultures, in Petri's dishes, have a piece of filter paper placed under the cover, which has been moistened with ten to fifteen drops of formalin. The plates are then placed in a closed vessel in the bottom of which is laid paper or cotton saturated with formalin. After twenty-four hours the cultures are fixed. Test-tube cultures are closed with a plug of cotton that has been wet with formalin and then placed in a closed chamber as above. After twenty-four hours they are removed and sealed with sealing-wax, when a permanent preparation is obtained. Colonies from plate cultures may be permanently mounted by the following procedure: The selected colony is cut out of the plate and placed on a slide and covered, and then a little of the melted medium is run under the cover. The slide is then exposed to the action of the vapor of formalin for twelve hours. Formalin renders ordinary culture media, gelatin, and that fluidified by bacteria non-liquefiable by heat. The above-mentioned method of preserving bacteria has been employed successfully by Alleger, Cheesman, and many others. I am informed by Dr. Cheesman that cultures treated in this manner by him a year ago are still well preserved, but some of the chromogenic forms have lost their color to some extent.

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Dr. HENRY POWER said that in his experience formalin had appeared to be very irregular in its action. He had noticed this especially in studying the minute anatomy of the cells.

The PRESIDENT asked if it had been found that the freshness of the tissues was an essential point in the successful use of this agent.

Dr. FREEBORN said that when formalin had been first brought into use he had directed the specimens to be placed in a two-per-cent. solution in the operating room, and this plan had yielded excellent results. Subsequently he had found the specimens very poorly preserved, and he had then increased the strength of the solution to five per cent. with rather better results for a while, but again there had been trouble. Finally he had adopted the plan of substituting a two-per-cent. solution of formalin for the water ordinarily employed in Müller's fluid. Since then he had used this "formalin-Müller's fluid," and there had been no trouble.

The PRESIDENT said that recently in preparing a specimen for the museum his attention had been directed to this matter. A heart had been mislaid, and had become quite foul before he had seen it. It was placed in a two-per-cent. solution of formalin, and notwithstanding the very bad condition of the specimen when placed in this fluid, it had been restored to nearly as good condition as if it had been immersed in alcohol or in formalin when quite fresh. He would like to ask whether Dr. Freeborn had noticed any effect on the diffuseness of the staining with the hæmatoxylin as a result of delay in putting the tissues in the formalin.

Dr. FREEBORN replied that he had noticed this diffuse staining in the amnion of some pigs where there had been a delay of three or four hours before immersion in the formalin solution. Kohn had experimented on a putrefying solution of peas, using various strengths of formalin, and he had found that anything above a five-per-cent. solution would sterilize and deodorize this fluid. Many other similar investigations had been made, with like results.

Dr. F. M. JEFFRIES referred to two mishaps with formalin in preserving the intestine. After the specimens had been placed in a two-per-cent. solution of formalin for about three days, they had turned black. He had been at a loss to account for this. Possibly it might have been due to some medication that had been used, but it had ruined the specimens.

Dr. THOMAS S. SOUTHWORTH said that he had placed a number of children's lungs in a two-per-cent. formalin solution for a considerable time, and had obtained a blackish-gray discoloration, which had not been entirely removed by alcohol. It was probably due to the length of time the specimen had been in formalin before being transferred.

Dr. FREEBORN said that a fœtal pig that had been put in a ten-per-cent. solution of formalin about eighteen months ago, still retained its white color beautifully. As formalin is an oxidizing agent, it was quite possible that something in the intestine had formed a dark chemical compound with the formalin.

Dr. POWER said that he had preserved fourteen specimens of intestine in formalin without observing this discoloration. They had not remained for any length of time.

Dr. EDWARD LEAMING said that formalin was used frequently in photography for the hardening of gelatine plates. The action of formic acid should be to reduce the silver salts, and he had found that this had occurred in unexposed plates. A similar reduction might occur with salts of other metals.

Dr. FREEBORN said that sometimes there was an over-oxidation of the methylic alcohol in the manufacture of formalin, by which formic acid was produced. He had also found that this oxidation would sometimes continue in open vessels, resulting in the formation of a considerable quantity of formic acid. Formalin was now manufactured by a number of firms. It had been put on the American market under the name of formulose, which apparently had an identical action with formalin.

IMPROVED STAGE FOR USE IN PHOTOMICROGRAPHY.

Dr. EDWARD LEAMING exhibited a new form of apparatus intended for use with the microscope in photomicrography, It was found in certain cases that in attempting to photograph a slightly uneven specimen, or a nerve cell with a long process, that it was impossible to get it all in the same plane with the slide held in the usual way. To surmount this obstacle, the apparatus exhibited had been devised by the assistant to Mr. Kraft, of this city. It consisted of a light framework and a light stage on which the specimen was clamped. By means of an ingenious screw adjustment the slide could be tipped in various directions, and across the axis of the lens.

REPRODUCTION OF PHOTOMICROGRAPHS.

Dr. LEAMING made some remarks on this subject, illustrating them with some beautiful examples of such work in colors. He said that the three-color photography by the gelatin process he had attempted to utilize in reproducing photomicrographs. The image was first focussed through a violet screen, and then negatives were taken successively through red, violet, and green screens. These are the complementary colors to the three colors in which the photograph is finally printed. The negative taken through the red screen is printed in blue, that through the green screen is printed in red, and that through the violet screen, is printed in yellow. The color screens are made of glass and tough collodion, properly colored. From these negatives three bichromate gelatin printing plates are obtained, and the printing done by superposition. Unfortunately, the manner of printing alters the results somewhat, and although this is of no importance in ordinary artistic work, it is a serious drawback to the use of this process for purely scientific purposes.

Dr. FREEBORN exhibited under the microscope the original slides from which the colored photographs had been made.

Dr. POWER said that he had taken a great deal of interest in this subject in connection with general photography. The want of registration is a difficulty with the printer, but probably there would be difficulty in the registration even aside from the fault of the printer, owing to the imperfections in our lenses, and the slight differences in the size of the images for the different colors. He thought it possible that changing the camera length might obviate this. A moderate amount of change in the length of the camera would produce only a very small change in the image.

Dr. LEAMING said that he thought Dr. Power was in error on this point, for, focussing to be of service must be done chiefly through the objective, and not by changing the length of the camera. It was more difficult to focus through a violet screen, but if this were done, the images would be more nearly perfect.

INSTRUMENT FOR CUTTING OFF THE SPINAL CORD.

Dr. PEARCE BAILEY said that in order to avoid the mutilation of the spinal cord which occurred when it was taken out in the usual way, he had devised an instrument, consisting of a small, slightly curved blade at *right angles* to the stem. This knife should be inserted some distance into the spinal canal, and the cord cut off at right angles. This also gave a much better specimen for making sections.

Dr. JAMES EWING thought the instrument should prove very useful. In removing the cord anteriorly it was usually very difficult to extract the last two or three inches, but with this new instrument this could be done from above.

PRESERVATION OF SPECIMENS OF THE INTESTINE.

Dr. HENRY POWER said that about one year ago he had presented to this Society a preliminary report on the preservation of the intestine. He had continued this line of experimentation since that time, using children as the subjects. At first, the best method had seemed to be the injec-

tion through a canula of a two per-cent. solution of formalin very slowly into the rectum. For the past year most of his experiments had been done with only eight or ten inches of pressure, and with a two per-cent. solution of formalin, both peritoneum and bowel being injected in the majority of cases. He had learned that one of the most important points in the preservation of the intestine was not to handle it. The formalin appeared to penetrate rapidly from the peritoneum to the mucous membrane; hence it was better to inject into the peritoneum. He had selected formalin because of its gaseous and penetrating nature. From three to five specimens had been taken from the various parts of the bowel, and they had been uniformly preserved, much better than in the usual way. In these experiments he had been assisted materially by Dr. Southworth. In one case, the injection had been made shortly after death, and the autopsy performed forty-three hours afterward. In another case, the injection had been made twenty-four hours after death, and the autopsy performed shortly after this, the intestine being found in a state of excellent preservation. He had found that the anatomical relations of the cells were excellently preserved, although the minute anatomy of the cells was not so good.

Dr. EWING said that in looking over these specimens he had been impressed with the marvellous preservation of the endothelial cells. The nuclei, the cell bodies, and the outlines between the cells could be easily distinguished. He had never seen this with any other method of preparation.

Dr. SOUTHWORTH said that Holt, in his article in *Keating's Encyclopedia*, stated that he rarely found the epithelium present if the autopsy were made more than six hours after death, and he expressed the belief that the desquamative catarrh was the most frequent form of acute intestinal disorder in children. This, the speaker said, he was inclined to doubt, for even where their autopsies had been made twenty-four hours after death, the epithelium had been preserved.

Dr. POWER then presented several

PHOTOMICROGRAPHS BY THE CARBON PROCESS.

He said that the great advantage of the carbon process was that the prints were entirely permanent. As the pigment was either a finely ground earth, or finely pulverized carbon, and the background apparently some form of lime suspended in gelatine, even the yellowing of the paper was avoided. He presented photographs of tissues done with an amplification of from ten to a thousand diameters, and of bacteria with an amplification of from seven hundred and fifty to one thousand diameters. He used monochromatic light with "critical illumination" from the sun, and the plate was backed with some substance which would not spread through the film, so that there would be no spreading of the image from the whites into the blacks.

Dr. MARY A. DIXON JONES presented four microscopical specimens illustrating what she considered to be a new form of degeneration of the ovary, by which most of the organ was changed to myxomatous tissue.

The Society then went into executive session.

Stated Meeting April 8, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

MALPOSITION OF THE KIDNEY.

Dr. G. A. TUTTLE presented a kidney which had been situated in the hollow of the sacrum. The renal artery was given off close to the origin of the middle sacral artery. This condition, the speaker said, was not extremely uncommon. In rare instances, it had been known to interfere with labor. An abscess of the kidney occurring in this abnormal situation would render the diagnosis obscure.

CYSTIC KIDNEY.

Dr. TUTTLE exhibited a kidney which had been removed from a man forty years of age, who had been brought to

the hospital in uræmic coma. At autopsy, the kidney had been found in a state of advanced cystic degeneration. There was practically no kidney tissue remaining. Such kidneys are always bilateral. The principal symptoms in these cases are those of Bright's disease—recurrent attacks of hæmaturia and albuminuria—and the patients always die in uræmic coma. These cystic kidneys are found sometimes enormously developed in the fœtus. Virchow had advanced the theory that this cystic condition in the fœtus was due to imperforate uriniferous tubules.

TUMORS OF THE KIDNEY.

Dr. TUTTLE presented several microscopical specimens of tumors of the kidney. He said that during the last five years, in the Pathological Laboratory of the Presbyterian Hospital, which received pathological material from that hospital and also from St. Luke's, there had been only ten specimens of primary new growths of the kidney. Six of these had been obtained by autopsy, and five out of the six had been discovered accidentally, having existed without symptoms during life. There was one tumor, a very large metastatic growth which could not be treated by operation, which caused the death of the patient. Of the remaining four specimens removed by operation, three were from the surgical service of the hospital, and one from an outside surgeon. The growths were from one-fourth to one inch in diameter in most instances, and were situated in the cortex of the kidney. Dr. Tuttle said that the exact origin and classification of primary tumors of the kidney had been a matter of much uncertainty. It was conceivable that tumors might originate in the epithelium of the pelvis, or in the tubules, or the connective tissue between the tubules, or in the blood-vessels. The structure of five of the tumors was as follows: (1) A pure lipoma, one inch in diameter, projecting above the surface of the kidney beneath the capsule. (2) A minute myoma composed of smooth muscle and some small round cells. (3) A small papillary ade-

noma consisting of a small cavity lined with cuboidal epithelium. (4 and 5) Two alveolar adenomata consisting of rounded and oval spaces filled with cells resembling gland epithelium, and some of these spaces presenting a distinct lumen. In places these tumors bore a slight resemblance to the tissue of the supra-renal capsule.

In Virchow's *Archives*, Bd. 93, was an article by Grawitz on the so-called lipomata of the kidney, in which it was stated that they were not rarely found accidentally at autopsy. The description corresponded with that of the adenomata just given. The author considered them to be portions of supra-renal capsule which had become enclosed in the kidney during fœtal life. The kidney at this period was more or less lobulated, and it was possible that portions could be caught in these clefts. In about one thousand autopsies at the Presbyterian Hospital, one case was recorded in which a small fragment of supra-renal tissue was easily recognized under the capsule of the kidney. Under the microscope, in one portion, it was separated from the tubules by a delicate connective-tissue capsule, and in another portion the two tissues had no dividing line. These fragments had been found in many other situations, *c. g.*, in the broad ligament, and in and about the testicles. The speaker said that it was very probable that these nodules did occasionally originate in this way from enclosed portions of the supra-renal tissue.

SARCOMA OF KIDNEY.

Dr. TUTTLE then presented specimens removed from a man forty-two years of age, who had had for the first time a slight hæmaturia shortly before entering the hospital. The next day there had been difficulty in passing urine, and then pain in the left lumbar region, radiating down to the left testicle and glans penis. After about five days, the urine had again become clear, and the pain had ceased. About two weeks later there had been a second attack of hæmaturia. A third attack with pain occurred just before

his admission. About six weeks before this a tumor had begun to grow from the right shoulder. Examination showed a large, hard mass in the left kidney, and the diagnosis was made of renal tumor with metastasis. At the autopsy there was found a dense mass weighing two pounds eleven ounces, and extending from the spleen to the brim of the pelvis, and from the floating ribs to the right border of the vertebral column on the left side. It was a new growth involving the left kidney. There were numerous metastatic deposits in the liver and lung, varying from one-fourth of an inch to two inches in diameter. Microscopical examination of these tumors showed a stroma of dense connective tissue, forming spaces subdivided into small, rounded alveoli. Some of these alveoli were completely filled with cells resembling epithelium, but the larger number showed the opening between the cells filled with blood. It was possible that a hemorrhage into a carcinoma might produce some of these appearances, but considering that all the metastases showed the same structure, one would be justified in calling this a sarcoma developed from the blood-vessels of the kidney. The tumor and metastatic growths were exhibited under the microscope. (Figs. 1 and 2).

PAPILLOMA OF THE KIDNEY.

The next tumor presented was from a male, thirty-six years of age, who had always enjoyed good health with the exception of rather frequent and severe headaches. One week before coming under observation, the urine had been noticed to be of a bright red color from the admixture of blood. There was no pain or ill health. Cystoscopic examination was made with almost negative results on account of the hemorrhage. The blood seemed to come from a point close to the neck of the bladder. Supra-pubic cystotomy was then performed. The bladder wall appeared normal except for a small ulcer at the fundus. Blood was seen to issue from the left ureter. No enlargement or tenderness of the left kidney could be detected. The left kidney was

removed, but the patient succumbed to the operation. The organ was moderately enlarged, and contained a number of large cystic cavities into which projected an abundance of papillary growths. The trabecular tissue was in part like dense renal tissue, and in part soft and gray. Under the microscope there were long, delicate filaments of connective tissue covered with epithelium, which closely resembled the epithelium of the pelvis of the kidney. The appearance of the tumor seemed to indicate that it started in the pelvis of the kidney.

ENDOTHELIOMATA (?) OF THE KIDNEY.

Dr. TUTTLE said that the most interesting specimens were two tumors, one of them brought to the hospital by Dr. F. Tilden Brown from a case reported in the Boston *Medical and Surgical Journal*, of April 18, 1895, by Dr. W. M. Swift, of New Bedford. The patient, a man, forty-seven years of age, after suffering for a short time with night sweats, noticed a tumor in the right side of the abdomen. When examined a few months later, he complained of pain in the right groin, a dragging sensation in the testicles, frequent and scanty micturition. A tumor, the size of a small cocoanut, was found in the region of the right kidney. It was slightly movable, and somewhat tender to pressure. The urine was normal in quantity. It was removed by operation, and recovery was perfect. The tumor was situated at the lower end of the kidney, and was completely encapsulated. It had apparently developed from the lower and outer part. (Figs. 3 and 4). The minute structure was the same as in the next tumor to be described, which had been removed at St. Luke's Hospital by Dr. Bangs in March, 1895. The tumor consisted of a number of nodules scattered throuh the kidney. The capsule was extremely vascular. Microscopical examination showed a mass of rather large cells, supported by slight, irregularly branching trabeculæ, forming in places fairly complete elongated alveolar spaces, while in other places, there was no alveolar arrangement.

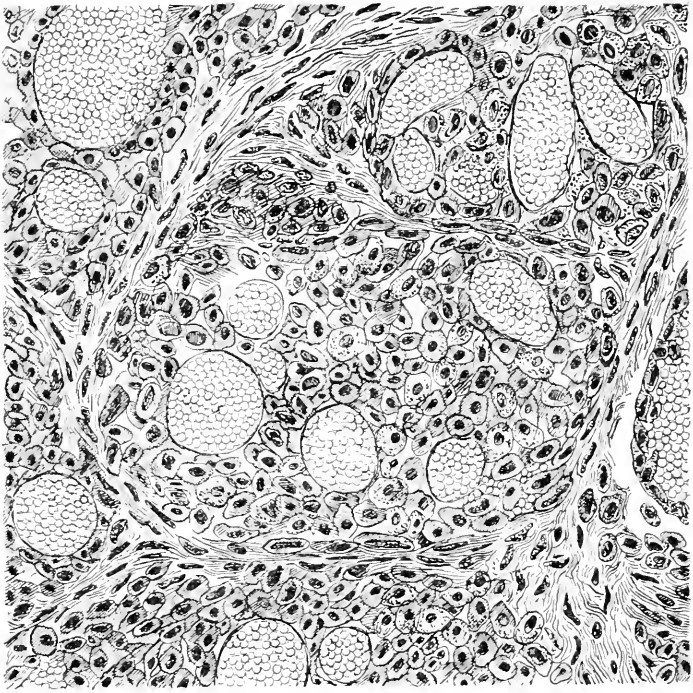

Fig. 1.—Angio Sarcoma of Kidney.

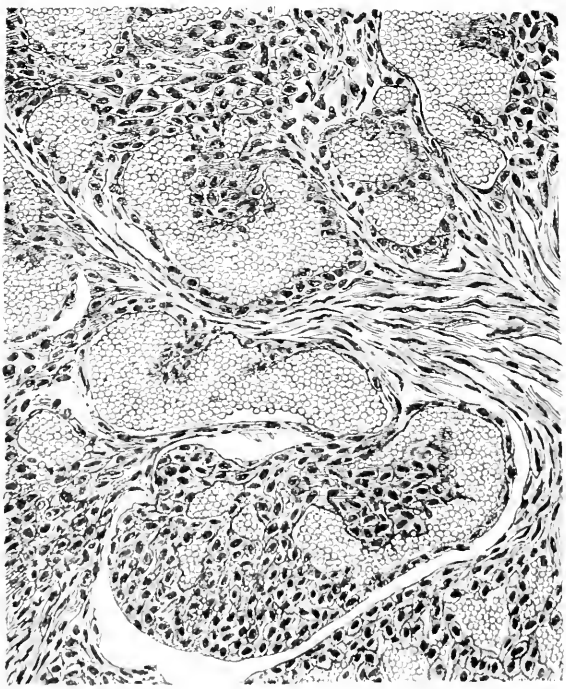

Fig. 2.—Angio Sarcoma of Kidney.

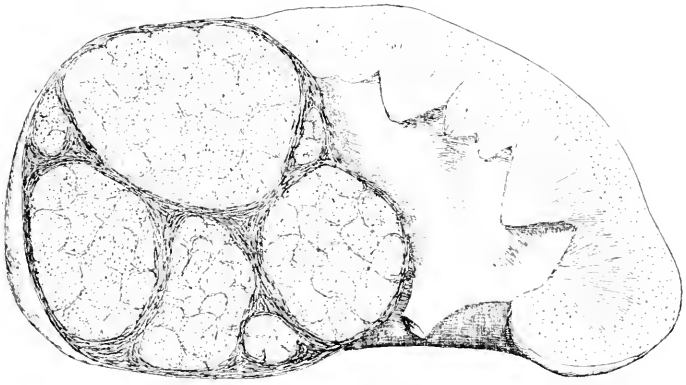

Fig. 3.—From Endothelioma of the Kidney (Dr. Swift's Case).

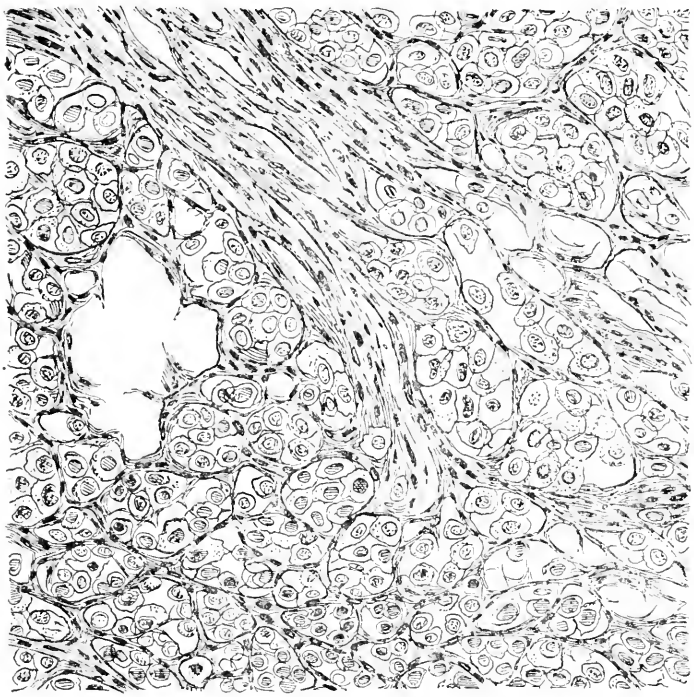

Fig. 4.—From Microscopic Section of Endothelioma of Kidney (Dr. Swift's Case).

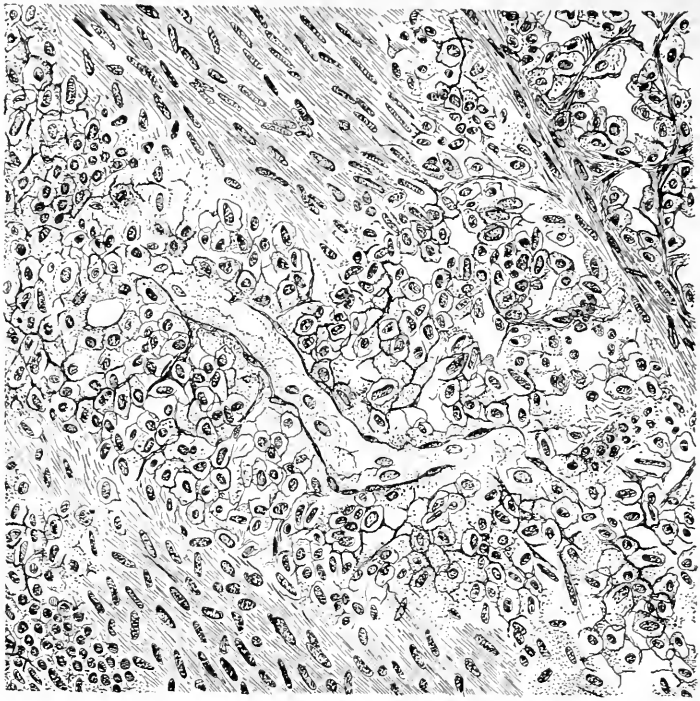

Fig. 5.—From Microscopic Section of Endothelioma of Kidney (Dr. Bang's Case).

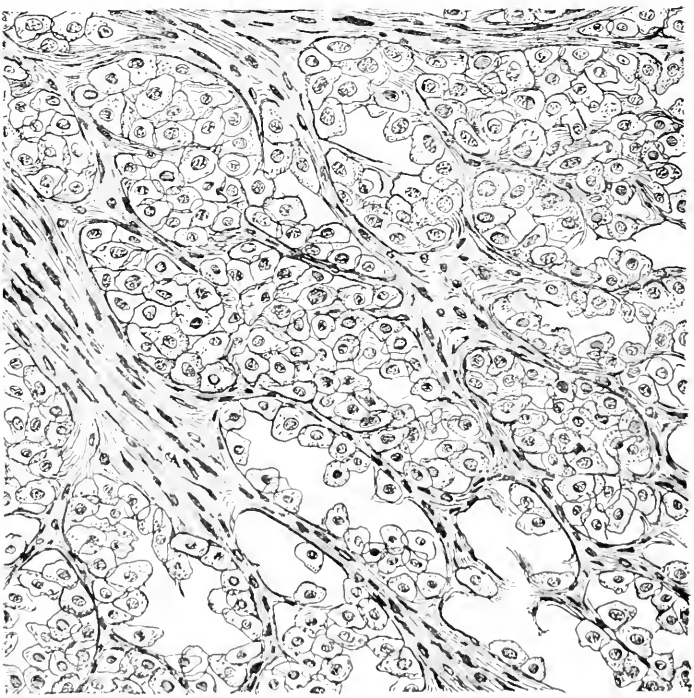

Fig. 6.—From Microscopic Section of Endothelioma of Kidney (Dr. Bang's Case).

The trabeculæ consisted of minute blood-vessels. In some places small areas of blood were seen surrounded by a very delicate but distinct limiting membrane. The tumor cells were rounded or polygonal with a sharply defined outline. For the most part, the cell protoplasm was homogeneous, and did not stain well with eosin. The nuclei were of medium size, and stained well with hæmatoxylin. The character of these tumors was still doubtful. Similar tumors had been described as carcinomata, or adenomata from the proper cells of the kidney tubules, and as endotheliomata developing from the endothelium of the perivascular lymph spaces. From the great vascularity of these tumors and the relation of the cells to the blood-vessels and the connective-tissue trabeculæ, the speaker said it seemed to him that they were more probably developed from the endothelium of the lymph tissue, as recently described by Hildebrandt. The cells of the supra-renal capsule were very liable to undergo fatty degeneration, and then would closely resemble the structure found in these tumors, with the exception of the great vascularity. Microscopical sections of these tumors were then exhibited. (Figs 5 and 6).

The PRESIDENT said that he could not bring himself to believe that the last specimens were endotheliomata. He was about to present a specimen in which the adenomatous type was very clearly shown.

Dr. GEORGE P. BIGGS said that in a specimen recently brought to him by Dr. Alexander for examination there was an encapsulated tumor, about as large as a medium-sized orange, projecting out a considerable distance from the kidney. The microscopical structure of this tumor was quite similar to that shown in the sections of the last tumors exhibited. In some places there was a perfectly regular adenomatous arrangement, and he looked upon his specimen as one of alveolar adenoma.

Dr. F. TILDEN BROWN presented microscopical specimens of what appeared to be

A TYPICAL ADENOMA OF THE KIDNEY.

The growth had been removed from a woman, sixty-two years of age, under the care of Dr. Kammerer. It had existed for eight years. On examination, it was found to be about the size of a child's head, very movable so that there was some doubt as to its being a neoplasm of the kidney. It was not particularly vascular, and was made up wholly of new growth with the exception of a little kidney tissue. The patient recovered well from the operation, but died after an attack of hemiplegia, some two or three weeks later. No autopsy was obtained.

ADENOMA (?) OF THE KIDNEY.

Dr. J. S. ELY presented a small portion of a tumor of the kidney, together with microscopical sections of the same. In structure it seemed to him very much like the two last cases presented by Dr. Tuttle. The tumor occupied the upper portion of the kidney, pushing the remainder of this organ downward and inward. It was very distinctly encapsulated and lobulated. The centre of the tumor showed an extensive area of degeneration, but the nature of this degeneration could not be determined. The whole tumor was soft, and contained much blood. There was no clinical history.

The speaker said that the most recent and complete article on this subject was by Lubarsch in Virchow's *Archives* for 1894. He endeavored to prove that they were of supra-renal origin, and he had collected twenty-nine similar cases, in all of which careful microscopical examination had been made. In his opinion, they had all developed from inclusions of the supra-renal capsule. The structure was as follows: A fine connective-tissue reticulum, consisting almost entirely of a slight adventitia of blood-vessels—on one side, slight endothelial lining, and on the other side, large cells, for the most part columnar in shape, with rounded ends, very clear protoplasm, rather large, distinctly

staining, oval nuclei, and a rather loose intra-nuclear network. The whole arrangement was distinctly alveolar, and the disposition of the clear, large-bodied cells was in most cases around a distinct lumen. The presence of the blood in these lumina had evidently suggested to Lubarsch that these were angio-sarcomata, but it seemed to the speaker that this could be just as well explained by supposing that it was the result of hemorrhage. Regarding the question of whether those growths originated from supra-renal inclusions or were adenomata of the kidney, this observer stated that the points in favor of supra-renal origin were: (1) The clear protoplasm of the cells, which distinctly resembled the protoplasm of the supra-renal body, and which was like the granulations found in the cells of the tubular epithelium; and (2) the presence of glycogen in the cell bodies and in the lumina. This, the speaker said, he had found in his specimen. Lubarsch had examined twelve tumors of the kidney, and in none of these had he been able to find glycogen. Yet he cited another observer as authority for the statement that the supra-renal body frequently showed the existence of glycogen. The distinct acinous arrangement and the nature of the nuclei of the cells, resembling as they did epithelial cells, would lead him to class this tumor as an adenoma or adeno-carcinoma, rather than an endothelioma, although he would admit the possibility of its being an endothelioma originating from the lymphatics. So far as he knew, glycogen was found in secreting cells—epithelial cells,—and this offered an obstacle to the theory mentioned. He had on a number of occasions distinctly seen glycogen in the tubular epithelium in cases of Bright's disease—at least the reactions which are supposed to be characteristic of glycogen were readily obtained. It should be stated, however, that this glycogen is not very soluble in water. With iodine it readily stains a deep mahogany-brown, and is digested and made to disappear under the influence of the ferment of saliva. Singularly enough, after treatment with iodine, the glycogen

becomes soluble in water, so that the subsequent manipulations of a specimen so treated must be carried on without contact with water.

Dr. ELY said that the difficulty was to define just what is an endothelial cell. Anatomists were inclined now to make no distinction between epithelial and endothelial cells. Personally, he had only seen what appeared to be undoubted endotheliomata in connection with the pleura and dura mater of the brain. In these cases there appeared to be a definite endothelial structure, and the cells, when teazed out, were flat, or irregularly shaped, with large nuclei with a loose open reticulum—a distinct endothelial arrangement. He did not think too much stress should be laid upon the shape and size of cells; one should depend rather upon the relation of the cells to the stroma than upon the cells themselves, for pressure alters greatly the shape of cells. It was well known that the cell body might differ very materially in different conditions of degeneration.

The Society then went into executive session.

Stated Meeting, April 22, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

TUMOR OF THE CEREBELLUM.

Dr. FREDERICK PETERSON presented a tumor of the middle lobe of the cerebellum, removed from a boy of twelve years, who had been sent to him for examination in July, 1895. About Christmas of 1894, up to which time the patient had been perfectly well, he had an attack of grippe with meningeal symptoms. After recovery from this he suffered from periodical headaches which grew worse. These headaches were frontal, occurred once a week, and lasted a few hours. Sometimes he was delirious during these attacks. Six months previous to coming under the observation of Dr. Peterson, he was said to have had optic

neuritis. The examination revealed the following: Optic atrophy with feeble perception of light; knee-jerks absent; no nystagmus; no ocular palsies; no paralysis or alteration of sensibility; pulse and respiration normal. He had attacks of headache with vomiting weekly A very peculiar symptom was constant choreiform movements of the head, mouth, and face muscles, and all four extremities, precisely like an ordinary chorea. There was a staggering gait. The diagnosis of a glioma or glio-sarcoma of the middle lobe of the cerebellum was made, the symptoms being typical. The boy, while on a visit at Syracuse some time ago, fell downstairs, fractured his skull, and died. Dr. Van Duyn, who made the autopsy, had kindly sent him the brain. On microscopic examination, by Dr. Bailey, it proved to be a glioma, and the situation of the tumor in the vermis was verified. The tumor was encapsulated, was 5 ctm. broad and 2.5 ctm. deep, and lay directly in the vermis, encroaching equally on each side into the lateral lobes of the cerebellum. The fourth ventricle was widely dilated, and the whole bulk of the pons seemed to have been subjected to considerable compression. Dr. Peterson said he had seen many cases of tumor of the cerebellum, but never before one with the choreiform movements which distinguished this case.

PRIMARY PERNICIOUS ANÆMIA.

Dr. JAMES EWING, in discussing this subject, reported the following illustrative case: The patient, a man of forty-five years, of American parentage, had been admitted on April 9, 1896, to the Roosevelt Hospital. His family history was negative. There was a moderate alcoholic habit, and some years before he had had symptoms of secondary syphilis. For five weeks prior to his admission it was stated that he had been very pale, and had suffered considerably from dyspnœa on exertion. There had been no disturbance of vision, no headache or dizziness, but for four weeks there had been œdema of the extremities, and he had lost a good

deal of strength. The urine was of dark color and scanty. On admission, he was markedly pale, but not jaundiced; the pulse was regular and small; the arteries were apparently normal; there was considerable œdema of the feet and legs. The splenic area was slightly increased. He was given arsenic and iron, but without benefit. On April 10th, the hæmoglobin was 25 per cent., and the blood-count showed 1,128,000 red blood cells. A dried preparation showed that the condition was one of primary progressive pernicious anæmia. The size and form of the blood cells were very characteristic. There were very fine microcytes, very large megalocytes, and gigantoblasts in abundance, and great variations in the intensity of the hæmoglobin stain. There was a considerable increase in the white blood cells, chiefly in the polynuclear leucocytes, and a moderate number of large myelocytes were found, On April 11th, he was given five minims of Magendie's solution of morphia to produce sleep. After this dose he went into profound collapse, and was with difficulty resuscitated. On April 13th he suddenly began to breathe very badly, and he died four hours later with symptoms of asphyxia.

The autopsy was made two hours after death. The lungs were emphysematous and extremely anæmic, except for some small areas of partial consolidation. The bronchial lymph nodes were slightly enlarged. The pericardial sac contained a few ounces of reddish fluid. The right heart was distended by a peculiar soft blood-clot. No other clots were found elsewhere, and it was evident that the coagulability of the blood was greatly diminished. The total quantity of blood also appeared to be diminished. The heart was nearly normal. The liver was enlarged, and very firm. The outlines of the lobules were very distinct, and the peculiar rust color of the organ was very striking. the spleen was markedly enlarged, weighing thirteen ounces. The kidneys were somewhat smaller than usual. The surface was granular, the cortex thin, the markings indistinct, and the whole organ somewhat congested. In the intestine there was an abnor-

mal adhesion binding the transverse duodenum down to the lumbar vertebræ, and producing a slight narrowing of the lumen. There was evidence of catarrhal enteritis, but there were no parasites present in the intestine. The bowel contents consisted almost entirely of mucus, giving a remarkably strong odor of hydrogen sulphide. The sternum, ribs, vertebræ, clavicle, humerus, and hyoid bone had been examined, and in all these situations there was very extensive increase in the marrow cavities and these cavities, were filled with red marrow. *Microscopical examination* showed in the spleen no increase of connective tissue, a marked diminution of cellular elements, both of the Malpighian bodies and of the spleen pulp. In many of the Malpighian bodies the small round cells were entirely wanting. A slight reaction for iron, hæmosiderin, was developed by potassium ferrocyanide and acidified glycerine, but it was much less marked than in the liver. There was no granular pigment observed as a result of the extensive destruction of the red blood cells in the spleen. The thyroid showed a very marked general thickening of the trabeculæ with partial atrophy of many alveoli. In the liver there was slight general increase of fibrous tissue between the lobules and between the liver cells. The liver cells showed marked fatty degeneration.

Both the nuclei and liver cells themselves were distinctly increased in number, and some of these new cells and nuclei were of very large size. Throughout the liver there was an abundant deposit of yellowish pigment granules, giving a very distinct reaction for iron. In the stomach there was a moderate grade of chronic catarrhal inflammation, with increase of connective tissue and atrophy, or dilatation of glands. In the lower dorsal and lumbar regions of the spinal cord, the only parts examined, there was slight sclerosis of the columns of Goll, but without pronounced atrophy of fibres in this region. Nissl's stain showed ganglion cells to be present in moderate degree an absence of chromophilic granules about the nuclei in many cells, while other cells showed extensive deposits of greenish pigment commonly seen after

middle life. The red marrow was found in all the bones examined—the ribs, sternum, vertebræ, clavicle, humerus, and hyoid. In all of these bones, the cancellous spaces were very much widened and filled with light red, semi-fluid marrow. The shafts or outer plates of these bones were distinctly thinner than normal. The head of the humerus could be easily crushed in by pressing on the cut surface of the cancellous tissue. No fatty marrow was seen in any of these bones. Cover-glass preparations were made from the various organs concerned in blood formation, and stained in Ehrlich's tri-acid mixture. As far as could be judged by this method, while the red marrow in all the bones contained a large number of megaloblasts, the total number of nucleated red cells was considerably less than is to be found in normal adult red marrow. In the preparation from the ribs, the nucleated red cells did not compose more than one-fiftieth part of the cells present. All the red cells, both nucleated and non-nucleated, seemed to number about one-eighth of all the cells in the marrow of the ribs and other bones. While, therefore, the locality of the formation was very much widened, it did not seem that the number of the red cells in active proliferation was correspondingly increased. The majority of the new cells in the red marrow consisted of small and large mononuclear cells, myelocytes, polynuclear neutrophile leucocytes, and eosinophile leucocytes. While the manufacture of red cells was here very widely distributed, it seemed that the total productive capacity was probably diminished rather than increased.

Dr. Ewing here illustrated his remarks by exhibiting charts and slides. The first showed the blood from a case of pernicious anæmia, with the characteristic megalocytes and the small basophilic granules in the megaloblasts. A chart of the blood from a case of chlorosis was also exhibited. Here the blood cells were moderately diminished in number, and there was a general diminution in the hæmoglobin. In this case one did not see in any quantity the large megalocytes of pernicious anæmia. A common form of degeneration,

the speaker said, was the extrusion from the body of the red cell of a mass of protoplasm, which stains with methyl blue, and which gives all the characteristics of the blood plate. A chart showing the characteristics of the blood of secondary pernicious anæmia was also shown, and the relations of this condition with primary pernicious anæmia were discussed.

The examination of such a typical example of pernicious anæmia, in which all the essential features of the disease were so strikingly developed, naturally suggested, Dr. Ewing said, some considerations regarding the etiology and pathogenesis of the disease. It was now generally admitted that pernicious anæmia is primarily a condition of excessive hæmatolysis rather than one of defective hæmatogenesis. While very acute cases of pernicious anæmia had been recorded in which the characteristic changes in the bone marrow, leading to defective hæmatogenesis, were absent, the disease seemed not to exist without excessive hæmatolysis. He had recently had an opportunity, through the kindness of Dr. Northrup, of examining an acute case, lasting only four weeks. In this patient, the red cells numbered less than 500,000 per cm. There was an almost entire absence of nucleated red cells of all varieties, and of abnormally large red cells, although degenerative changes in the red cells were extensive. While no autopsy was made, the observations of Ehrlich had shown that such cases were unattended by the usual changes in the bone marrow. As evidence of the excessive destruction of red blood cells in pernicious anæmia, one might refer to: (1) The abundance of degenerative changes in the red cells; (2) the coloration of the plasma as seen in dry preparations; (3) the deposit of large quantities of iron in the liver and spleen; (4) the appearance of excessive pathological blood pigments, and of an excessive amount of iron in the urine; and (5) in the acute cases, the very rapid diminution in the number of red cells in the blood.

But these facts were not conclusive proofs that excessive hæmatolysis was the sole factor in the production of the disease. Degenerative changes in the red cells are abundant

in chlorosis, and in secondary anæmia, when the number of red cells is not markedly reduced, and when iron is not always present in excessive amount in the liver or in the urine. Neither is the presence of an excess of iron in the liver a positive indication that pernicious anæmia has existed. In a series of examinations of 44 livers taken as the cases came to autopsy, Russell found in 7 quite as much iron as Hunter found in the liver of pernicious anæmia. These were cases of marked secondary anæmia, from cancer, tuberculosis, and other diseases, and the patients had not suffered from pernicious anæmia. In those cases of pernicious anæmia which follow pregnancy, it was difficult to see what could be the toxic agent which could alone initiate and continue a fatal destruction of red cells. Even more difficult was it to explain those cases which follow large hæmorrhages by the assumption that there is present in the blood a toxic agent which continues the destruction of red cells. An examination of the clinical aspect of the disease seemed to show that according to their etiology there were cases of pernicious anæmia which were very probably caused by a toxic agent circulating in the blood, and destroying red cells, and that there were other cases which could be most reasonably referred principally to defective hæmatogenesis. In the first class might be placed those examples of the disease which were associated with the presence of intestinal parasites, or blood parasites, such as the *cercomonas globus*, or the malarial organism ; also, the cases following infectious diseases. Of the idiopathic forms, while the very acute cases, unattended by marked changes in the bone marrow were most naturally referred to excessive hæmatolysis, it was difficult to see how a toxic agent destroying red blood cells could, in a few weeks, have produced changes in the bone marrow of such enormous extent as were found in the case just reported. It was much more probable that an abnormal process of cellular proliferation, leading to defective hematogenesis, was the chief factor in the production of the blood changes in this case. It would appear, therefore,

that both excessive hæmatolysis and defective hæmatogenesis were essential features of the pathological process in pernicious anæmia, and that sometimes one, and sometimes the other was the more prominent. The speaker said that a large number of studies had been undertaken with a view of determining the nature of the toxic material which destroys the red cells in pernicious anæmia. The studies of Hunter in this direction were important. In an article in the *British Medical Journal*, February 8, 1896, he reported some recent experiments, and supported his previous conclusions that pernicious anæmia is a specific form of blood destruction, occurring chiefly in the portal circulation, and caused by the absorption of the products of intestinal bacteria. Cadaverine and putrescine he regarded as the probable agents concerned. Jurgenson had reported a case of pernicious anæmia cured by the removal from the intestine of enormous numbers of the *bacterium termo*, and Liebman had produced a condition of chronic blood poisoning resembling pernicious anæmia, by the intra-venous injection of hæmoglobin, of glycerine, and of pyrogallic acid. He believed the disease to be due to hæmo-globinæmia. The followers of the Dorpat School believe that the poisonous agent in the blood of pernicious anæmia comes from the destruction of both red and white blood cells. The nervous origin of pernicious anæmia had received some little support. Some of the cases reported, like the present one, showed changes in the central nervous system, but in no instance did these changes appear to be of more than secondary importance. The theory most widely accepted was that the disease represented a rapid form of blood destruction, associated with a reversion of the blood-forming function to the embryonal type—in other words, it represented a tumor formation in a fluid tissue. This analogy to a tumor formation, however, appeared to be much more applicable to leucæmia than to pernicious anæmia. A comparison of the blood of fœtal vertebrates with that of pernicious anæmia certainly did show many points of resemblance, but the likeness did not seem to him to be especially striking.

Dr. THOMAS S. SOUTHWORTH said that in examining cases of pernicious anæmia, he had met with difficulty in diagnosis owing to the intermediary class of cases. Many cases were diagnosticated clinically as acute, primary pernicious anæmias. He had come to rely upon two things, viz.: the existence of the megalocytes—the large non-nucleated red cells,—and the presence of the megaloblasts—the oval, large nucleated red cells. Unless these were present in considerable numbers, however, the diagnosis could not be positively made.

Dr. SOUTHWORTH then exhibited microscope slides illustrating these points, and presented microscopical specimens from a case of

RACHITIC ANÆMIA.

He said, in January of the present year, a baby of eighteen months, with marked evidence of rachitis, had been admitted to the Babies' Hospital. The spleen had extended to the left anterior superior spine and measured 3 by 2 inches below the ribs. The liver had been enlarged, coming down one and a half inches below the ribs. There had been, also, some enlargement of the superficial glands. The number of red cells had been 5,144,000 to the cubic millimetre, the ratio of the white to the red cells being 1 to 168. The most interesting point in this case was the extremely large number of megaloblasts.

Dr. EWING asked Dr. Southworth as to the relative frequency of the severe forms of pernicious anæmia in connection with rachitis. He said that while he had found a great variety of severe forms of anæmia in connection with rickets, he had not observed progressive pernicious anæmia.

Dr. SOUTHWORTH said that he had seen many cases of profound anæmia, and the condition had yielded to the usual anti-rachitic remedies and tonics. In the case just reported the anæmia was not particularly marked, as there were over five million red cells.

PERNICIOUS ANÆMIA.

Dr. CHARLES FISCHER also presented a microscopical specimen from a case of pernicious anæmia. There was no clinical history. The patient had been in the hospital only three weeks. At the autopsy no other lesions had been found. The specimen showed all the varieties of degeneration that had been described by Dr. Ewing.

The Society then went into executive session.

Stated Meeting, May 13, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

A NEW METHOD OF PREPARING THE BLOOD FOR CLINICAL PURPOSES.

Dr. LOUIS WALDSTEIN said that since the work of Ehrlich and his followers, attention had been drawn again to the granules that are found in leucocytes, of which Max Schultze gave a description long before the studies of Ehrlich on this subject. Since that time the examination of blood with a view of determining the nature and the number of these granules had entered the clinical field, and had become more important as a diagnostic method. The method of Ehrlich and his followers was more especially one that could be applied in the laboratory only, as it required certain special apparatus, and considerable time was needed to perfect the coloring. A number of other investigators had, however, given their attention to this clinical method, among others, Hardy and Kanthack in England, a number of investigators in Germany, and Dr. Ewing in this country. Dr. Ewing had originated a method which came very near to the ideal one. During last year, the speaker said, he had devoted considerable attention to this subject, and in the *Berliner klinische Wochenschrift*, of April of last year, he had published the description of a method which,

with some modifications, he desired to describe and demonstrate this evening. All the various methods had for their principal object the rapid and perfect fixation of the blood. The more perfect and the more quickly this was done, the better. Heat, when applied in various ways, did this in a more or less complete manner, but often the flame and the incubator were not at hand at the bedside, and hence he had resorted to the fumes of osmic acid. He had used this agent previously in some studies that he had made under Ranvier, in Paris, in 1881. But there was a disadvantage connected with this plan—*i.e.* the longer the blood was subjected to the fumes of a four-per-cent. solution of osmic acid, the less would it take up the coloring agent. Last summer, in England, he had made some unsuccessful experiments with formalin, but since that time he had had more encouraging results with this agent. He was now able to prepare a satisfactory slide in six or seven minutes, and this preparation could be kept and examined at leisure. The method was so simple that even the nurse could spread the cover-glass for the physician. He believed the time would come when the blood would be examined just as commonly and systematically as the pulse and temperature are at the present time. There was a certain school of pathologists in Berlin which thought that we had reached the limits of cellular pathology, but he felt confident that the time was coming when cytology would be extended into the profounder study of the blood corpuscle during life, and that here we would find as important information as in the chemical and biological investigations of serum.

It is most essential that the slides upon which the blood-smears are made, should be perfectly clean, and it is well to this end to wash them with alcohol and ether, equal parts. The puncture for obtaining the blood is best made with a spear, such as is used by the dermatologists for the treatment of acne, for it will not be necessary to squeeze the finger or ear too much. A fraction of a drop of blood is caught up by the end of a smearing-slip, which is placed at

an acute angle on the slide and drawn over its surface with a gentle pressure as soon as the drop has run along the entire edge of the slip. These slips (Mr. William Krafft, 411 West 59th St., New York has them on sale) are made of crown glass, measuring 3 x 2 1/2 x 1/8 inch, with edges ground perfectly smooth and rounded. The slide is then immediately placed, blood downwards, over the mouth of a bottle containing a ten-per-cent. solution of formalin (twenty-five-per-cent. of the commercial formalin, which is a forty-per-cent. solution), and allowed to remain there from three to five minutes which is long enough to fix the blood elements. These specimens can be colored at once, or kept any length of time for further treatment. It is advisable to use only "Grübler's alcoholic eosin," as the ordinary eosin differs greatly in staining quality as well as solubility when coming from different factories. For the close study of the two varieties of granules stained with eosin, the best fluid is one containing eosin to saturation in eighty-per-cent. alcohol, to which is added an equal part of alcohol of the same strength. The smears are treated with this solution during two minutes, and then washed with water, and allowed to dry in the air, and inclosed with Canada balsam, which should not, however, be dissolved in xylol or benzol. That dissolved in cedar oil gives the best results. Besides the large "Eosinophile" granules, the smaller ones are also distinctly colored; they are, therefore, as well as the former "Acidophile," a fact to which attention had already been called in the before-mentioned article, and which had also been found by Hardy and Kanthack ("Oxyphile"). Ehrlich designates them as "Neutrophile" granules, because he found that they take up both acid and basic aniline dyes. Although it was not the purpose of this communication to enter upon a discussion of the granules themselves, it might be mentioned that when basic dyes are applied to such specimens previously stained with eosin, these smaller granules take up the basic dye in proportion to the time of exposure to their action. Methyl-blue, for instance, will

show them violet at first, blue at a later stage, and lastly, it will have neutralized the red entirely, so that the granules will be entirely discolored. The eosin acts evidently, in respect to the basic dye, as a mordant, much as in the case of cotton in the dyeing industry. Cotton is dyed by an acid color, but not by a basic dye. But if the acid dye be used first, it is found to act as a mordant; the cotton thread is thus provided with what the dyer calls an "acid back." The small acidophile granules also take up what the dyer calls "substantive dyes," just as does cotton. It is possible, therefore, that these so-called neutrophile granules are bodies resembling carbo-hydrates, and may thus be chemically different from those bodies which take up the basic dyes, *e.g.* the nucleus and other forms of granules. The large acidophile or eosinophile granules are readily saturated with acid dyes, and will not, therefore, take up any basic dye when once colored with an acid dye, provided that the basic-dye solution employed does not contain a certain proportion of alcohol, when other conditions prevail.

As a basic dye, the speaker said, he used for its distinctive qualities, both with regard to the staining of the nucleus and certain differentiations of the basophile granules, thionin—not the thionin of commerce—but what is also known as the "violet of Lauth." It is also called the thionin of Hoyer, because Hoyer used it in 1890 in his investigations of mucin. The speaker recommends the following staining fluid: Anilin water, two parts; 95 per cent. alcohol, one part; saturated with thionin. Anilin water is used because it makes the coloring permanent. The specimens are exposed to this solution for two minutes, thoroughly washed with water, allowed to dry in the air, and inclosed in Canada balsam. Thionin is an excellent nuclear stain, and produces peculiar coloring in certain blood specimens, which are to be treated of on a future occasion. It imparts, for instance, a brownish color to the large granules found in leucocythæmia. Under certain conditions the serum would be of a bluish tinge, and the red disks would be colored from blue to light green, de-

pending upon certain degrees of anæmia. For these reasons, his dye was a very valuable one. The best plan was to stain one slide with the eosin, and the other with thionin. That the formalin instantaneously fixed the blood was demonstrated by the fact that in certain cases the "budding" of the leucocytes was well shown.

From a number of indications the speaker ventured to conclude that continuous and systematic examinations of the blood during the entire course of the disease would lead to most interesting results from which might be ascertained important information, not only concerning the action of the toxines in infectious and other acute diseases, but also symptomatic changes in reference to their treatment. He would, therefore, recommend that such blood-slides should be made by the attendants quite as regularly as the records are taken of the temperatures, pulse, and respiration. At all events he should continue his work along these lines, and hoped to be able to report upon it at some future time.

Dr. JAMES EWING said he had examined a number of specimens stained by this method, and considered it a most excellent one. The method of spreading the blood was in itself a distinct advantage over the ordinary technique, in that the specially ground slide was more easily handled than the cover-glass, and the blood was spread more uniformly. It seemed to him even superior to the method of dropping the blood on one cover-glass and spreading it on another cover-glass, for Dr. Waldstein's plan gave a good opportunity for the formation of rouleaux. The fixation he had found to be very simple, and in every way satisfactory. He had tried Ehrlich's tri-acid mixture in addition to Dr. Waldstein's coloring agents, and he had come to the conclusion that the tri-acid mixture was the best of all. He had found that in the method of fixing by formalin the corpuscles were rather more yellow than when fixed by heat. Ehrlich's dye itself was not a very good nuclear stain, and in specimens fixed by formalin the tri-acid mixture did not stain as well as when the fixation was secured by heat. The blood plates

were, however, rather better stained after the formalin fixation than after heat. The thionin stain was certainly a most valuable one. The whole method certainly called for a very careful and extended trial by every one interested in the study of the blood.

Dr. J. S. THACHER asked if the length of time the blood was exposed to the formalin was of importance.

Dr. WALDSTEIN replied that he had not found any bad effect from prolonged exposure to formalin, but one or two minutes sufficed for the purpose of fixation.

"AN EXPERIMENTAL STUDY OF SOME OF THE NUTRITIONAL CHANGES RESULTING FROM FAT STARVATION."

Dr. C. A. HERTER presented a paper with this title. He said that this experimental study had been originally undertaken to determine if the lesions of rickets could be produced in growing animals by withholding fats as far as possible from their dietary. This was suggested by the fact that the clinical indications of rickets were often promptly made to disappear by the addition of fat to the food. The pig was selected for these experiments.

Pig 1 was experimented upon for a period of fifty-one weeks, beginning December 16, 1893. It was given a limited quantity of milk from the Walker-Gordon Laboratory. The average proportion of fat in this milk was one-fortieth per cent., whereas the milk of the sow usually contains from eight to ten per cent., and ordinary skim-milk of the cow, one per cent. of fat. At the end of the first week, notwithstanding the fact that the animal was receiving about 1/300 part of the normal proportion of fat for a pig, its weight increased, so that at the end of the fifty-one weeks the total increase in weight was 16 pounds. The animal became markedly constipated, and, after a few weeks, showed great muscular weakness, and the skin and hair became dry. Towards the end of the term of experimentation, the animal became very weak and drowsy; then the temperature rose, and it was evident

that it was moribund. It was therefore killed. It was found that the hæmoglobin had been reduced to 65 per cent., and that there was a slight reduction in the number of red cells. "Pig 8" was fed on the same milk, but was allowed to take as much as it desired instead of a limited quantity. At the end of twenty weeks, the animal showed some muscular weakness and a tendency to drowsiness. "Pig 2" was experimented upon for fifty-six weeks. It was given a supplementary diet of carbo-hydrates. Towards the end of the experiment the urine was at times saccharine. The fæces were dark, and sometimes diarrhœal. The skin remained soft and well nourished. Towards the end there was slight muscular weakness noted.

An inquiry into the pathological anatomy of the changes in the skin principally, showed that there was no subcutaneous fat, but instead a layer of gelatinous material. In all the parts of the body where fat was normally located this gelatinous material was found. In Pig 2 some shrinkage was found in the fat cells after eight weeks, and after fourteen weeks they were shrunken to half their normal size. At the end of twenty weeks the fat layer was very pale and the fat cells reduced in size, but there was no gelatinous material such as was found in Pig 1 and Pig 8. The heart was large, pale, and flabby; there were several hemorrhages on either side of the coronary arteries; instead of the usual fat layer was one of gelatinous material. Many of the muscular fibres of the left ventricle were the seat of slight granular degeneration. The histological appearance of the liver was normal. The kidneys were surrounded by the same gelatinous material, and these organs were enlarged and contained hemorrhagic spots. The epithelium of the tubules everywhere showed granular degeneration and the cells of the secreting tubes were swollen and degenerating —in short, the kidneys presented the appearance of parenchymatous degeneration. The supra-renals appeared normal except for being unduly large. The knee joints were filled with bloody synovial fluid. The cranial bones were

thinner and more brittle than normal. The bone marrow was replaced by material having the consistence and appearance of blood-clot. Sections from the femur showed normal bone structure. In Pig 2 the femur showed a development of bone almost exactly the same in degree as in Pig 1, the marrow adjacent to the compact bone being very red, while the rest was of the normal pink color. A chemical examination of the gelatinous material showed it to be evidently a phosphorus-containing proteid, known as a nucleo-albumen; hence, the process already described might be properly described as a "mucoid degeneration." An inquiry into the quantity of urea and phosphoric acid, and the ratio between the two, resulted in showing that there was a very considerable increase in the amount of urea excreted in the course of the experiment, but there was not a corresponding increase in the excretion of phosphoric acid—indeed, there was a slight decrease. The striking feature was the high ratios throughout, or, in other words, the small quantity of phosphoric acid excreted in proportion to the urea. In Pig 9 there was an irregular but slight increase in the phosphoric acid. These animals were fed on fatless milk, and in all the proportion of phosphoric acid was distinctly lower than in the animals fed on normal milk. On feeding Pig 9 with an additional allowance of suet, there was an immediate return to the ratio normally observed in pigs fed on normal diet. This would seem to prove that the low phosphoric-acid secretion was the result of the defective absorption of phosphorus from the intestine. Notwithstanding the great diminution of fat, the quantity of phosphorized fat—the lecithins of the brain—was not diminished. In endeavoring to study minutely this process of mucoid degeneration, it was found that the cells broke up into larger and smaller fat globules; then the cells diminished in size; the cell membrane grew irregular in outline, and in time the cell contents were free from fat. The findings in Pig 2 show that this withdrawal of fat from the milk did not necessarily cause this mucoid degeneration. The chronic degeneration of

the kidney in Pig 1 probably resulted from the prolonged activity in excreting nitrogenized material, owing to the highly nitrogenized diet. This view was confirmed by the results in Pig 2, where there was much less nitrogenized food, and no such changes were found in the kidney.

The following were the author's conclusions:

(1) That the lesions resulting from fat starvation in pigs do not resemble rickets; (2) that prolonged fat starvation leads to the disappearance of fat from the adipose tissue of the body, and its replacement by a gelatinous homogeneous-looking substance; (3) that this substance contains a nucleo-albumen, but not mucin; but the pathological change may be spoken of for the present as mucoid degeneration; (4) that the lecithins of the brain and liver are not materially reduced by fat starvation; (5) that fat starvation does not lead to mucoid degeneration if the animal be given a large excess of carbo-hydrate food; and (6) that fat starvation causes a very imperfect absorption of phosphoric acid from the intestine.

Dr. ALEXANDER LAMBERT asked if the paralysis appeared to be due to a general weakness, or to a nerve lesion.

Dr. HERTER replied that he thought it was due to the local atrophy of the muscle fibres. The nerves, however, were not examined.

Dr. REGINALD H. SAYRE asked if the hindlegs alone were paralyzed in these animals?

Dr. HERTER replied that all four legs were affected, but the hindlegs suffered more severely in Pig 1. They were about equally affected in Pig 8. As to the question of fat starvation and its bearing on rickets, he would say that the appearances were more like those of scurvy than of rickets. He had examined the breast milk from women nursing rickety children exclusively, and had been surprised to find that in some of these the milk was exceedingly rich in fat, and in none was the fat below the average.

Dr. WALDSTEIN said that in a rather large clinical experi-

ence he had seen many rickety children, and he had never been impressed with the idea that there was a causal connection between the proportion of fat in the milk and rickets, but he had been impressed with the fact that many children were rachitic whose mothers had been chlorotic or markedly anæmic during the period of pregnancy. He could recall several instances in which the same mother had had both healthy and rachitic children, and in every instance the mother had been anæmic during the time in which she had carried the child which had subsequently developed rickets. He had made many inquiries on this point, with results of a similar tenor. Moreover, he had not found that the use of cod-liver oil was of benefit in rickety children. The only valuable treatment, in his experience, for rachitis, had been the administration of phosphorus in olive oil emulsion, according to the method of Kassowitz. He had not obtained such results from the use of Thomson's solution of phosphorus. He recalled having seen in lipomata of old people a gelatinous condition answering the description of mucoid degeneration, as given in the paper.

Dr. JAMES EWING said he had repeatedly seen the fat about the heart and kidney in cases of acute phthisis replaced by a gelatinous material.

The Society then went into executive session.

Stated Meeting, May 27, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

DILATED STOMACH SIMULATING ASCITES.

Dr. C. N. DOWD presented a greatly enlarged stomach, taken from a patient who had presented the usual signs of ascites, with flatness on percussion in the dependent portion of the abdomen, no matter what position the patient was in, and tympanitic resonance above. There was also a small nodule in the right hypochondrium. The patient was doing

badly and an exploratory incision was made to determine whether she would be benefited by any operative procedure. An enormous stomach was found to occupy practically the entire abdominal cavity extending into the pelvis below and pushing out the abdominal walls on each side. There were several quarts of fluid swashing about in it and this with the gas which was also there gave the signs of ascites. It was impossible to pass a stomach tube. The patient made a good recovery from the ether but died at a later time of inanition. The pyloric thickening was cancerous.

SCOPE OF THE WORK OF THE NEW YORK CITY BOARD OF HEALTH.

Dr. HERMANN M. BIGGS said that he had been connected with the Health Department since 1887, at the time of the first of the recent cholera outbreaks in this city. Dr. W. M. Smith, the Health Officer of the Port, had requested him to make a bacteriological examination to establish the diagnosis of cholera. Dr. Prudden was associated with him in this work. This was the second time that such an examination had ever been made for the purpose of diagnosticating cholera. Shortly afterward, at the request of Health Commissioner Bryant, they had been made bacteriologists to the Health Board. The disinfecting station was then established. In the fall, at his suggestion, a memorial was presented to the Health Board, regarding the restriction of pulmonary tuberculosis, but so much opposition was made by the medical profession that nothing was done except in an educational way. At that time, only one prominent medical practitioner supported the view that pulmonary tuberculosis was a communicable disease, and that the Health Board should take steps looking towards its restriction. In 1892, when a number of cases of cholera actually gained entrance to this harbor, it became possible to get money for the establishment of a bacteriological department. A resolution was introduced by Dr. Bryant, and passed De-

cember 18, 1892, establishing the Division of Pathology, Bacteriology, and Disinfection. In 1893, a system of house disinfection and disinfection at Sixteenth Street were put in force, and means for the transportation of articles secured. An outbreak of typhus fever soon put the new system to a severe test. In January, 1893, the speaker said he presented a communication suggesting the appointment of a bacteriological diagnostician for diphtheria, and naming Dr. W. H. Park as a suitable person for the position. He was appointed in April, 1893, and the work in the bacteriological diagnosis of diphtheria was begun. In 1893 and 1894 the temporary corps was kept on duty. In the spring of 1894, his investigations in Berlin into the question of the value of diphtheria antitoxin had so impressed him with the value of the new treatment that on his return he urged the Board to enter upon this work.

A special appropriation of $3500 was made in January, 1895, and the permanent force of the laboratory was then considerably increased, mounting in the year to a total force of thirty-one. In another communication, he had recommended that some steps be taken towards the control of pulmonary tuberculosis. Arrangements were early made for the free distribution of diphtheria antitoxin. Experiments had also been carried on regarding the tetanus antitoxin, the testing of the virulence of bacilli found in throats which were apparently simple angina, etc. Dr. Huddleston had recently carried on experiments to determine the best methods of producing vaccine virus. Last summer, Dr. Alexander Lambert studied this subject in the large cities of Europe, and as a result of all this it was decided to adopt the fluid virus. More than 30,000 diphtheria cultures had been examined during the past year; about 2000 examinations of sputa for tubercle bacilli had been made by Dr. Fitzpatrick; about 500 vials of antitoxin had been produced weekly. The discovery of diphtheria antitoxin fortunately furnished a plea for securing money from the Board of Estimate and Apportionment, which could be used for the es-

tablishment of a research laboratory. None of the largest cities in this country, he said, was at the present time without a bacteriological laboratory for use in connection with the Health Board. The money collected from the sales of antitoxin here had been sufficient to very materially assist in the scope of the work.

MIXED INFECTION AND VIRULENCE OF DIPHTHERIA BACILLI.

Dr. W. H. PARK said that he had been deeply interested in the question of mixed infection because of the important bearing of this subject on the antitoxin treatment of diphtheria. He presented temperature charts of three children affected with laryngeal diphtheria. In the first case, between February 11th and 19th, the temperature had ranged between 105° and 105.5° F. The glands had become swollen four days before death, and the pneumonia which had been present, had become more marked. The autopsy showed broncho-pneumonia, and lesions of the kidneys and other organs. The cultures from the lungs showed numerous streptococci, as well as Loeffler bacilli. The cultures from the neck were nearly pure growths of streptococci. Cultures from the blood of the various organs showed pure growths of streptococci. When these streptococci were injected into a rabbit, they were found to be of moderate virulence. His experience had been that after passing the streptococci through a few rabbits, they increased somewhat in virulence, but then the virulence remained stationary. The second case was a child of one year, with laryngeal diphtheria, and high temperature. It was given antitoxin. Twenty-four hours later, it was intubated, but after three hours and a half the tube was removed. Thirty-six hours after admission, the temperature was 106° F., and remained high until death. The child remained a large part of the time in a position of opisthotonos. The lung showed a late stage of broncho-pneumonia. Cultures from the lungs and other or-

gans gave streptococci. The third child had been sick only two days, but the chest was full of râles. There was no membrane in the throat, but there were some diphtheria bacilli present. The temperature at the end of forty-eight hours reached 107° F., and the child died. The autopsy showed both lungs consolidated. Cultures from the lungs and from the blood showed the pneumococcus, and a few colonies of diphtheria bacilli were found in the cultures from the lungs.

Cultures from the blood of those dying early in diphtheria, without high temperature, were usually sterile; when there was a high temperature, septicæmia was generally found. When the lungs showed lesions, diphtheria bacilli were always present in the consolidated areas. Streptococci were also found. The diphtheria bacilli were found in the blood only twice in 14 cases.

It had been suggested by Dr. H. M. Biggs, that the work done some time ago regarding the virulence of the diphtheria bacilli be again tested. In cases in which the clinical diagnosis was follicular tonsillitis or pseudo-diphtheria, the virulence of the cultures was tested, and notes made regarding the number of diphtheria bacilli and whether or not they were characteristic. In four months, 71 such cases had been tested, and from 50 of these bacilli were obtained in pure culture, and inoculated into guinea-pigs. In 38 of the 50, the bacilli were characteristic and abundant; in 37 they were virulent; in 1 non-virulent. In 2, the bacilli were atypical. Out of 48 characteristic cultures, the bacilli were virulent in 46, and non-virulent in 2. In 2 cultures of the pseudo-type, they were virulent. Of those tested, in 26 the diagnosis was not diphtheria, and of these, 22 were virulent, and 4 non-virulent. In 24 doubtful cases, the bacilli were virulent in 22, and in 2 not virulent—in other words, in 12 per cent. of the 50 cases, they were non-virulent. In 2 of these, the bacilli would be called atypical.

Dr. L. WALDSTEIN asked Dr. Park if he had noted any relation between the size of the individual links and the lengths of the chains, and the virulence of the bacilli; also

whether in making cultures of the streptococci the virulence was effected by the alkalinity or acidity of the medium.

Dr. PARK replied that he had examined swabs from slight pus cases, and in these the chains had been very long. In some of the cultures from the severer cases the chains had been rather short. He had made no exact observations as to the effect of the alkalinity of the medium on the virulence of the bacilli.

TETANUS ANTITOXIN.

Dr. ALEXANDER LAMBERT said that he had been trying for three years to get a culture of tetanus bacilli which would retain virulence sufficiently to allow him to investigate the tetanus antitoxin. Finally he had obtained a culture, .1 cc. of which would kill a guinea-pig in five or six days. It then occurred to him that as, clinically, tetanus was usually a mixed infection, it might be well to try mixed cultures. He had, therefore, mixed the tetanus bacillus with the *bacillus rosaccum metalloides*. The result was that a guinea-pig promptly died in tetanic spasms. Following out this line of investigation, he was soon able to get a toxin, .001 cc. of which would kill a guinea-pig in two days and a half. He was now able to obtain from the horse a tetanus antitoxin, 1 cc. of which would kill 3,350,000 grm. of guinea-pig. Apparently, two and a half to three times the equivalent of antitoxin was necessary to protect the animal from a fatal dose of toxin. The antitoxin already obtained was of therapeutic strength, and he believed it would soon be placed by the Health Board upon the same commercial basis as diphtheria antitoxin.

Dr. GEORGE P. BIGGS said that he had found that the antitoxin animals were capable after a time of taking enormous quantities of the toxin. The doses taken now by some of the animals under treatment the longest, were 500 cc. at a time. It had been found that new horses could be made within four to six weeks to yield an antitoxin of high strength, whereas formerly it was thought that three

months were required. The expense of production was thereby much lessened, and a higher grade of antitoxin obtained. Very few of the horses this year had died under the treatment with toxines. He had made autopsies on many of the cases dying at the Willard Parker Hospital, but no new lesions had been found in the cases treated by antitoxin.

The PRESIDENT asked if any lesion had been found in the horses that had died, which would explain the death, or their susceptibility to the toxines.

Dr. BIGGS said that autopsies had been made, but nothing had been found to explain the varying sensitiveness of different animals.

VACCINE.

Dr. J. H. HUDDLESTON said that the virus was collected from heifers, two to four years old. Clinical tests could alone furnish a guide as to the quality of the virus. Experiments were made to determine in what part of the vesicle the living germ was present, using for this purpose, five young children, and vaccinating them in from three to five places. The vaccinations were successful in all of these children, and it was found that the base gave the best results, and the serum the poorest, although it was the latter that had been usually employed on quills and ivory slips. Other comparative tests showed that the younger the animal, the better the results, and the more nearly typical the eruption. In practice, heifers, two to three months old were found to be best, all things considered. It had been found that a small area covered with well-developed vesicles yielded as much as a larger area, because on these the vesicles were not usually so numerous. The area selected was usually the posterior portion of the abdomen and a short distance on the inner surface of each thigh. The maximum quantity of lymph was obtained just before the vesicle became a pustule—in other words, usually four or five days after vaccination, but there was a considerable individual variation in the animals. If several vaccinations were made

on the calf at intervals of a day, the later vaccinations, as in the case of a child, would be found to mature much more rapidly than the first ones. Continued experiments had shown that the liquid virus gave a higher percentage of successful vaccinations in the proportion of 71 successful vesicles by the dried virus to 100 of the latter. The best method of preservation had not yet been determined. Experiments had been made of mixing it with lanoline, with glycerine, and with chloroform water, and glycerine and water. The lanoline seemed to be the best preservative of the vaccine, but the glycerine had more power to limit the number of bacteria in the vaccine. The receptacles for the virus consist of small stoppered glass vials. The virus is so thick that it is with great difficulty that it can be drawn up into capillary tubes. The heifers are examined by a veterinarian, and if found healthy, are kept for two or three days before vaccination. There is no advantage in previously disinfecting the skin with sublimate solution, for it must become infected again before the time for removing the virus. When the vesicles have properly developed, the parts are thoroughly cleansed, and the pulp taken and passed through a rolling machine, and at the same time mixed with glycerine. The average product from each of 50 recent calves, was 16.5 cc. By using a small spear-shaped lancet, and moistening the point with the fluid vaccine, one quick puncture is sufficient to complete the vaccination. The vaccination made in such a way yields a small, typical vesicle, with a small areola, and causes the patient scarcely any discomfort. There seemed to be considerable evidence to show that a single inoculation was not as complete a protection against small-pox as it had been supposed to be. An inspection of a number of these scars showed them to be so minute that they might be after a time easily overlooked.

THE EXAMINATION OF TUBERCULOUS SPUTUM.

Dr. CHARLES B. FITZPATRICK said that the method of staining that he had employed was that described by Gunther. In this Ehrlich's anilin-water fuchsin solution was

used for the coloring agent, and a three-per-cent. solution of hydrochloric acid in alcohol as the decolorizing agent. The bacilli by this method were stained a very distinct red. Examinations made in eight cases of influenza during the past winter failed to show the presence of any specific bacillus. In many instances the examinations of the sputum showed a mixed infection—a few tubercle bacilli with perhaps a streptococcus infection. On the disappearance of the mixed infection, it was often reported by the attending physician that the patient showed marked general improvement. The addition of 24 parts of English salt to a half-per-cent. solution of carbolic acid acts with the same efficiency as a preservative as does a five-per-cent. solution of carbolic acid, and it does not coagulate the sputum into balls.

The PRESIDENT said that for several years he had entirely abandoned the use of strong acid solution. He would take about eight ounces of alcohol, and drop into it a few drops of sulphuric acid. This formed an excellent decolorizing agent, although perhaps somewhat slower in its action than the stronger solutions. Nuttall had found that many of the tubercle bacilli were decolorized by strong acid, and proposed the use of this weak acid decolorizing solution.

Dr. FITZPATRICK said that with a simple mixture of alcohol and water one could remove enough of the primary stain to admit of the application of the secondary stain to the bacilli.

Dr. WALDSTEIN said that in the decolorization of smears it was not important to have the acid dissolved in water, but in staining sections the solution should be an aqueous one, in order to avoid the shrivelling of the sections.

ISOLATION OF DIPHTHERIA ANTITOXIN.

Dr. MILLER said that so far he had been unable to fully corroborate the interesting experiments of Brieger on the isolation of the antitoxin. The essential point was the separation of the antitoxin as a zinc compound. It seemed to

be especially difficult to completely separate it from the albumen.

The Society then went into executive session.

Stated Meeting October 14, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

MALFORMATIONS.

MALFORMATION OF THE GENITAL ORGANS; PROBABLY A CASE OF TRUE HERMAPHRODISM.

Dr. CARL BECK, present by invitation, presented specimens taken from an individual, twenty-one years of age, upon whom he had performed laparotomy last June. The patient died of pneumonia sixteen days later. One specimen showed a well developed penis, with the exception of the urethra, in the place of which was a slight depression. There was an infundibulum very closely resembling the introitus vaginæ. The membrane covering this was easily broken through, and disclosed a vagina and an infantile uterus. The patient stated that he had been regarded as a girl up to his seventeenth year, and that he had had sexual connection from the fifteenth year. He then assumed the male attire. There had been no menstruation, according to the history. At the time of the operation, which was done for the removal of two pelvic tumors, it was found that the removal of the larger growth was very difficult on account of extensive adhesions. The two tumors filled up the small pelvis, the larger one reaching up as high as the umbilicus. The pedicle of each tumor was rather thick, and was attached to the peritoneum about half an inch laterally from the symphysis, and about a quarter of an inch below the os pubis. Dr. Beck said that he had a distinct impression that on the right side an ovary could be felt, but just as he was endeavoring to examine into this point more

carefully, the patient's respiration suddenly ceased, and this abruptly terminated the examination, and also the operation. Unfortunately, the autopsy had been performed in his absence, and many interesting points had been consequently overlooked. The pathologist, Dr. Brooks, reported that the tumor consisted of mixed elements, making it impossible to classify it. The bulk of the growth was composed of embryonic tissue, and the tumor apparently belonged to the teratomata. He had shown these tumors to several eminent medical gentlemen, and none of these had cared to express any distinct opinion on the question of whether these growths were testicles or ovaries. No seminal vesicles had been found. Dr. Torek had informed him that this patient had been admitted to the Skin and Cancer Hospital last year, and had been treated by Dr. Fox for syphilis.

Discussion.

The PRESIDENT said that the decision as to the actual sex in this case depended upon whether these tumors were ovaries or testicles, or whether one was an ovary and the other a testicle. Such cases had been reported. An examination of the specimen seemed to him to indicate that the case was one of pseudo-hermaphrodism of the male type, with failure of union of the lateral halves of the body at the time of the completion of the external genitals, and with the persistence of the remnants of the Müllerian duct, which ordinarily becomes atrophied in man, but which in the female is developed into the uterus and Fallopian tubes. In a number of cases of masculine pseudo-hermaphrodism, uteri of about this size had been described as a result of the persistence of a portion of the Müllerian ducts. In a case like this, in which positive evidence was lacking, the fact that the definite function of the male had been performed, should have considerable weight in reaching a decision. Certainly, the penis in this case bore a much closer resem-

blance to the true penis than to a hypertrophied clitoris, although Ziegler pictures a hypertrophied clitoris which very closely resembles the organ found in this specimen.

Dr. H. J. GARRIGUES, present by invitation, said that in order to understand these cases of hermaphrodism, whether true or false, we must go back to the history of development. Before the tenth week we could not distinguish the sex at all. It should be remembered that the development takes place from three different localities, viz.: (1) For the outer part the starting-point is the genital tubercle and genital fold; (2) inside of that are the Müllerian and Wolffian ducts. The former develops into the Fallopian tube and uterus in the female; the other duct becomes the vas deferens in the male, and is often found as a remnant in women. (3) The sexual glands are developed from the epithelium covering the Wolffian body. Bearing these facts in mind, he said, it was evident that any one of these three parts could assume the type of the opposite sex. In spurious hermaphrodism, there is only one sex, and there is an opposition between the outer part and the inner part. In true hermaphrodism, there must be at least one testicle and one ovary. A microscopical examination was necessary to prove a case one of true hermaphrodism. So far as he knew, there was only one reported case of true hermaphrodism—*i. e.*, one in which there had been a microscopical examination to confirm the diagnosis. This was an infant, who lived only one month. In this case, there were two testicles and two ovaries, and the nature of all of these organs was demonstrated by microscopical examination. There was no difficulty, he said, in understanding how one sexual gland might take the male type and the other the female type, nor in understanding how the glands might both belong to one sex and the external genitals to the other; but how could there be both ovaries and testicles? The explanation probably was to be found in the different origin of the stroma of the testicle and the ovary. According to Waldeyer, the seminal canals of the testicle were formed by

invagination from the Wolffian ducts, while the follicles in the ovaries were formed from the germ-epithelium.

Dr. GARRIGUES said that he had seen the two tumors in the case under discussion, just after their removal from the patient, and hence, while in the fresh state; they had appeared to him to be sarcomata. He had also had the opportunity of examining the patient while alive, and had in this way been able to diagnosticate an entirely normal virginal uterus. A certain journal had made the statement that these cases were quite common, but this seemed to him a gross exaggeration. For twenty-five years he had been in the habit of making a considerable number of examinations, and he had never seen a specimen as well developed as this one. He had measured the uterus in this case, and had found it two inches and a quarter deep. On the left side was an entirely normal ovarian ligament, one inch and a quarter long, which had been abruptly cut off. The same was true of the broad ligament on that side. On the other side, the post-mortem knife had left only short tabs to indicate the site of these parts. In his own mind he felt sure that this was a case of true hermaphrodism, and hence he regretted exceedingly that a minute examination had not been made. He knew of an individual, now alive, who not only menstruated, but possessed semen. The left side of this individual looked like a male, and the other side like a female.

Dr. J. F. ERDMANN, present by invitation, said that he had also seen the specimen. He could not add materially to the report of this case, but desired to refer to an interesting clinical history recently sent to him, which bore on the subject under discussion. The patient was about twenty-five years of age, and had all the appearance of a female as regards the mammary development, and all the appearance of a true hermaphrodite as regards the development of the genitals. In the labia majora on both sides were what appeared to be testicles, and there was also a vagina. The patient would not submit to an examination with the finger or with a sound. He stated that he had had sexual connec-

tion after the manner of the male sex. Recently, a specimen had been shown in the Genito-Urinary Section of the Academy, which was really an example of the false type of hermaphrodism.

Dr. BECK, in closing, said that he had personally had very little doubt that this case was one of true hermaphrodism. It was not certain that there had not been menstruation in this case, for the patient might have had it and denied the fact. The fact that this patient had had a chancre—the initial lesion of syphilis—on the male organ would also be in favor of the opinion that this organ was a true penis.

Dr. THOMAS S. SOUTHWORTH presented a specimen of CONGENITAL OCCLUSION OF THE BOWEL.

The child was one of twins, and died when five days old. The other twin died, after two hours and a quarter, and the autopsy showed congenital pulmonary atalectasis. In the child about to be presented, there had been no asphyxia at birth. On the first day a little mucus had been passed from the bowel, and also vomited. On the third day, there having been no further discharge from the bowel, castor oil was given, without effect. On the fourth day, there was a little vomiting, but there was no fæcal odor to it. The little finger was passed a short distance into the rectum, and a catheter was also introduced in the same way. The only result of this examination was the discharge of a long string of mucus. Just before death, on the fifth day, there was fæcal vomiting. Post-mortem examination showed the lungs fairly well aëreated, and the heart normal. The stomach was distended with gas, and its greater curvature was turned upward by the distended intestine. The peritoneum contained from four to six drachms of bloody fluid, and a few stringy clots. The small intestine protruded from the abdomen on making the first incision. The small intestine and the vessels of the mesentery were injected. The intestine was distended with a yellowish fæcal matter. The

lower part of the ileum was green and contained meconium. The diameter of the gut at the point of greatest distension was about three-fourths of an inch. In the ileum, and about two inches above the cæcum, the bowel was filled with a rather firm mass of fæcal matter and mucus. Below this, the ileum was contracted and nearly empty. A probe could be easily passed through the ileo-cæcal valve. The cæcum was exceedingly small, and the appendix was normal. The colon varied from one-eighth to three-eighths of an inch in diameter. The rectum was a little larger, and admitted the little finger up to the first joint. It was connected to the sacrum, and appeared to have been torn from its attachments. This probably accounted for the bloody fluid found in the abdomen.

The speaker said that cases of congenital occlusion were rare. It had been stated that only two cases had been found in the Vienna Hospital, in over one hundred thousand children. There might be: (1) an abnormally short or double bowel: (2) a double cæcum and appendix; (3) abnormal positions, due to unusual length of the mesentery, to hernia through the diaphragm or transposition of the viscera; (4) congenital absence of portions of the gut, a condition generally met with in poorly developed and acephalic monsters; (5) the stenosis might exist in the form of one or more rings. Atresia is only a more advanced condition. The most frequent sites are the beginning of the rectum, the end of the rectum, at the duodenum, and at the lower end of the ileum. Occlusion might also occur from anomalies connected with the omphalo-mesenteric duct. The persistence at the umbilicus of a portion of this duct might give rise to "mucous polyp of the umbilicus," or it might result in a blind pouch extending out of the ileum. Sometimes there was only a cord extending from the ileum to the umbilicus.

The etiology was briefly summarized as follows: (1) the duct may be occluded by a fold or diaphragm of mucous membrane, a condition which is most common in the duodenum or jejunum; (2) such malformations are ascribed to

arrested fœtal development, or to accidents in development; (3) the occlusion may be due to fœtal peritonitis; (4) it may arise from changes in the peritoneum in early fœtal life, resulting in adhesions or constricting bands; (5) there may be obstruction at the junction of the ileum and omphalo-mesenteric duct, due to an excessive twisting of the umbilical cord—an increase of the normal condition at this point. If the twist extends to the intestine itself, atresia occurs. In the case just presented, the stenosis was about two inches above the ileo-cæcal valve, and there was very imperfect development of the entire large intestine.

A NEW MORPHOLOGICAL ELEMENT IN THE CONES OF THE RETINA—"THE KUTTARASOME BODY."

Dr. IRA VAN GIESON said that the cones of the retina had been studied only as regards their shape and form. Max Schultze, in 1869, had so well described the cones, not only in the retina of the human subject, but in some of the lower animals, that very little had been added to our knowledge for about twenty years afterward. Then the connection of these cones with the central organs and with the ganglion cells of the retina was perfected. The cytology of the cone up to the present time had been almost entirely neglected. It had been his fortune to secure the retinæ from criminals executed at Sing Sing, and hence it had been possible to obtain them in a very fresh condition. They had then been stained by Nissl's method, and examined according to the most recent and approved methods. Unless done in this way, the object to be descried could not be seen. A striking body had been found just at the neck of the cone. It was composed of a series of parallel bars, and presented a gridiron appearance. These bars have lateral anastomoses, and at the top join in a semicircular manner. For this reason he had given this body the name of the "Kuttarasome body." This body was to be taken as the analogue of the chromophylic granules in the gang-

lion cells. He would also call attention to the fact that the material composing this body extended up into the cone itself in the form of lines.

Dr. J. S. Ely, by means of diagrams and photographs, described :

A CASE OF FISSURE THE ABDOMEN, PUBIC REGION, AND GENITALIA.

The appearance of the child was that of one in good health. It was the third child, the two previous children having been healthy. There was an indefinite history of an attempt at early abortion, followed by slight hemorrhage. The labor occurred June 26, 1892, and the presentation was R. O. A. The umbilical cord was so short as to cause some delay in the labor. The child died about twelve hours after birth. At the autopsy, the development was noted to be that of a child at full term. There was talipes varus of both feet, and the abdominal wall and genitals were malformed. From about 3 ctm. below the xyphoid cartilage down to the usual situation of the symphysis pubis was a large gash, measuring 8 ctm. from above downwards, and 7 ctm. laterally, and having an elliptical shape. In the edge of this defect in the abdominal parietes, a membranous pouch protruded forward. In this pouch a large part of the liver and small intestine could be seen and felt. From about the centre the umbilical cord originated, and was of normal diameter. The development of the genitals was exceedingly abnormal. A small wart-like prominence was seen in the median line, about 5 mm. in both diameters and of a bluish-red color. Just external to this was a slit-like opening, about 6 mm. in length, from which meconium could be pressed by pressure on the gut through the thin-walled omphalocele. At the same time, meconium passed in small quantity from a small opening just above the wart-like mass. In each groin was a reddish mass, about 2 ctm. long and 1 ctm. at the broadest part. The lower part of this mass was composed chiefly of

a reddish thin membrane. Towards its inner border was a small round opening, through which a probe passed into a larger cavity. Above and externally, this mass in the groin was made up of denser tissue. Below this mass was a slender protrusion, 1 ctm. long, and somewhat resembling in appearance the labium minus. Below this was a rounded prominence, covered with tissue like skin, and resembling slightly the labium majus. Below this was a small depression. On opening the abdomen by a median incision, the upper and anterior portion of the liver was found loosely adherent to the sac of the omphalocele. There was no evidence of a urachus. The liver was rather large, somewhat irregularly lobulated, and situated on the right side of the abdomen. The spleen was somewhat enlarged; it was situated normally, and its structure was also normal. The stomach had the usual situation, size, and shape. The small intestine was normal in size and attachments, but at the lower extremity of the ileum it was adherent to the anterior abdominal wall at a point corresponding to the small median opening already described. A probe passed from this opening into the lower portion of the ileum. The ileum also communicated by an opening in its right wall with the caput coli. This last was of normal size, and to it was attached the vermiform appendix. It was, however, almost spherical, and formed a sac about 2 ctm. in diameter. It represented all that there was of a large intestine. This cloaca-like pouch was closely attached to the posterior abdominal wall by a very slight mesentery. The ureter passed almost straight downward and communicated with pyriform bodies extending upward from the prominences in the groin. These pyriform bodies were alike on the two sides. Each of these bodies was about 4 ctm. long, broad below and circular throughout in cross-section. The lower portion was soft and hollow, and was lined by a somewhat wrinkled mucous membrane. The upper three-fourths of the body was hard, but contained a very small cavity, and resembled the uterus. It communicated below with the vagina by a

well-marked cervix. From the upper and outer side of this uterine mass a tortuous Fallopian tube ran upward to the vertebral column. It had a distinct fimbriated extremtiy. Each pyriform body represented a hymen, uterus, tube, and ovary, and the ureter on each side opened into the vagina on the corresponding side. The pelvis was rudimentary and defective in form. The ischium was represented only by a small knob. The ileum was well formed.

Dr. ELY then presented three specimens showing deficiency of the anterior abdominal wall. He said that where there was absence of bladder and of the pubic bones there was apt to be complete fissure of the genitalia, the ducts developing on their respective sides, but never fusing.

Discussion.

Dr. C. N. DOWD said that it was noticeable that almost all of these deformities were due to a failure of one of the ordinary processes. In one of the specimens, there were various amniotic bands and adhesions. It would seem quite possible that many of these deformities were due to such bands. We could not but grant their existence, and having done this, many malformations could be explained by such mechanical obstruction to growth. He had found that there were very few cloven feet on record—one such had been shown in the specimens just exhibited. In all the reported cases there had been a failure of development in the middle of the feet. It was easy to understand how such a cleft might result from amniotic bands. In all the cases he had been able to study, there had been an absence of one or more of the bones of the tarsus.

Dr. W. B. NOYES said that in contradistinction to a purely local cause, such as amniotic bands, he would call attention to a series of cases where the monstrosities occurred in families, showing a distinctly hereditary element. For instance, certain families were known to have cretins, associated with deaf-mutism, or with supernumerary digits, or something of the kind. Unless this could be explained as a coincidence,

it was difficult to understand their occurrence on the theory of a purely local cause.

Dr. DOWD said that it could not be denied that there was a hereditary element, particularly in regard to the occurrence of supernumerary parts. The mechanical explanation, however, applied to a certain number of the cases of failure of development.

Dr. GEORGE P. BIGGS thought that a band of sufficient size to produce such marked disturbances of development ought to be represented by some remnant. This would indicate that there must be something more than the bands to explain the condition.

Dr. DOWD replied that if the arrest of development occurred at a very early period of development, it would not be necessary to suppose the existence of very large amniotic bands.

Dr. ELY said that there could be no question that amniotic bands had much to do with the occurrence of certain very marked malformations; nevertheless the theory did not seem necessary to explain the failure of union of the two lateral halves of the body, or such phenomena as cleft hands or cleft feet. It was well known that the respective halves of the hands depended for their development upon the respective sides of the forearm. If, for example, the thumb were absent, the radius would be frequently found to be absent. It seemed quite possible to suppose that some maldevelopment, such as an interference with the nutrition of the cells which usually united the two lateral portions in the median line, might result in this class of malformations. It was now known that certain malformations could be produced by irritation of the embryo. The cytologists were able to state very early in the development the exact part which would result in the formation of the respective systems or divisions of the body. It was evident, therefore, that certain cells were set apart for the formation of certain definite parts of the body.

The Society then went into executive session.

Stated Meeting, October, 28, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

Dr. F. M. JEFFRIES presented a specimen from a case of

COLLOID CARCINOMA OF STOMACH AND OMENTUM.

The patient, a man, forty-eight years of age, had enjoyed good health up to two months prior to his admission to hospital, on September 17, 1896. At that time, he began to suffer from persistent nausea and vomiting, and the abdomen was observed to be larger than usual. While in the hospital, he complained of headache and shortness of breath, and had a short, dry cough. He died on September 26th. At the autopsy, the entire peritoneum was found to be covered with small nodules. These nodules involved the peritoneum covering the diaphragm, the mesentery, and even extended down into the pelvic cavity. The liver, spleen, and pancreas were normal. About three-fourths of the wall of the stomach was thickened with this same growth, which apparently had its origin in the pylorus. Both the lungs were quite adherent to the diaphragm. Microscopical examination proved the nodules to be colloid carcinoma.

Dr. JEFFRIES then presented specimens from a case of

CARCINOMA OF PANCREAS AND LIVER.

The patient, a laborer, forty-eight years of age, was admitted to hospital on September 12, 1896. His health had been excellent up to about three months before, when he began to experience pain in the right hypochondriac region. This was soon followed by enlargement of the abdomen and considerable loss of flesh and strength. On admission, the patient was very weak, and the skin was dry and yellowish. There was no cough or expectoration, and the heart and lungs were normal. The abdomen was distended with fluid. The lower border of the liver could hardly be felt. The urine was yellow. The clinical diagnosis was carcinoma of

the liver. At the autopsy, the right lung was found to contain many white nodules, varying in size from a pin-head to a pea. There were a few such nodules in the other lung. The liver contained many white nodules, varying in size from a marble to that of the fist. The largest one was at the free border, above the gall-bladder. The gall-bladder contained one large gallstone and two small ones. An impacted gallstone, half an inch in diameter, was found in the cystic duct. There was a large nodule in the head of the pancreas. The spleen and intestines were normal. The kidneys were much congested. The pancreas seemed to have been the first organ involved.

PERFORATION OF THE STOMACH.

Dr. JEFFRIES also exhibited specimens from a third case, the history of which was unfortunately very meagre. The patient, a German, about thirty-five years of age, had been admitted to the Trinity Hospital on October 23, 1896, and had died on October 26th. It was stated that on October 18th he was suddenly seized with severe abdominal pain. On his admission, a diagnosis of appendicitis had been made, and an exploratory operation performed, but the latter had failed to disclose any appendicitis, or reveal the true condition. The autopsy showed a general peritonitis, and also peritoneal adhesions uniting the liver to the diaphragm. On separating these adhesions, a cavity was discovered, the floor of which was formed by the stomach and half of the upper surface of the liver. The cavity was lined with considerable exudation, apparently indicating that the process was older than would appear from the history. There was also a perforation into the stomach, but the opening was round and smooth, and there was little evidence of inflammation here. The interesting question was as to the length of time that this had existed, and whether such a thick capsule as constituted the wall of this cavity could have been formed in seven days.

Discussion.

The PRESIDENT referred to a similar case presented to the Society a year or two ago, in which there was about the same thickening and involvement of the stomach, but in which the carcinomatous condition had been confined to the stomach.

Dr. MARY PUTNAM-JACOBI thought that the history and appearances of the case just presented agreed fairly well with those of a typical round ulcer of the stomach, with perforation and localized peritonitis. Microscopical examination of the tissues around the perforation might be interesting, as possibly disclosing thromboses and explaining the nature of the perforation. The first acute attack of pain probably coincided with the occurrence of the perforation. Such adhesions, she thought, could form in seven days.

The PRESIDENT was of the opinion that the only way to settle the question about the capsule would be to determine by microscopical examination just how much old connective tissue was present.

GIANT CELLS AND THEIR MODE OF FORMATION.

Dr. CHARLES A. VALADIER exhibited under the microscope a section from a giant-cell sarcoma of the tibia. It had been taken from one of the specimens in the laboratory of the College of Physicians and Surgeons, and was presented because it exhibited some interesting features of giant cells. In some places, these giant cells seemed to show protoplasmic processes, and at other places, retractions of the protoplasmic mass, looking like pseudostomata. He had concluded that they were in the act of embodying some of the surrounding sarcoma, and further study of the specimen seemed to confirm this view. On looking up the literature he had found that the question of the origin of giant cells and their significance in a tumor were much disputed. The fact of phagocytic action was mentioned by one or two observers, but more especially in regard to foreign particles, rather

than micro-organisms. Two interesting experiments were mentioned in Virchow's *Archives*, of giant cells found not only in tumors but also in normal granulation tissue in wounds. They had been produced experimentally by placing small pieces of cotton, catgut, and hair under the skin of animals. After a short time the granulation tissue which grew around these exhibited giant cells, and these had such phagocytic action that they not only embodied in their mass certain portions of hairs, but also the pigment of the hair. The other experiment consisted in placing two small pieces of cover-glass with a capillary space between them, in the omentum of a frog. Here giant cells also developed. The author believed that the inflammatory process set up by these foreign bodies drew to the parts leucocytes, and the welding of two or more of these leucocytes caused the development of giant cells possessing phagocytic action. Dr. Valadier said that he had seen these giant cells in epitheliomata and sarcomata. Their presence in sarcomata had been explained as having been derived from the osteoclast, but on this point there was much difference of opinion. He would like to raise these questions, viz.: Are these cells, as shown in the specimen, due to irritation within the tumor, as, for instance, from the presence of pigment? Might not the giant cells obtain their nuclei from the phagocytic action of these pseudopods?

Dr. J. S. THACHER said that he had found giant cells so frequently present in various inflammatory processes, particularly where there were small pieces of foreign matter, such as bits of sponge and dressings, that in the laboratory they had come to speak of these as "foreign body giant cells," in contradistinction to those found in tuberculosis. He had come to believe that giant cells were produced by irritations of various kinds; they were sometimes very abundant in a simple surgical wound. They usually differed from the giant cells of tuberculosis in that the latter had their nuclei arranged peripherally and had a necrotic centre.

Dr. GEORGE P. BIGGS said that he had also observed giant cells very commonly, but those apparently of pure inflammatory origin were usually somewhat smaller than the true giant cells—they might be perhaps better described as multinuclear cells.

Dr. THACHER replied that the cells he had referred to were certainly as large as the cells usually described as true giant cells.

Dr. LOUIS WALDSTEIN said that the more one observed giant cells under different conditions, the more one became impressed with the fact that they might have different origins. Those that he had seen in tuberculosis of glandular structures, such as the testicle and the kidney, had given the impression of being the product of a necrobiotic process—a fusion of cells which had gradually lost their distinct individuality. Then again, there were other giant cells, such as in the sarcomata and other neoplasms, which gave the impression of the body of the cell being still alive —as if there were multiplication of nuclei. Again, one was struck by the fact in tuberculosis, as well as in the cases referred to by Dr. Thacher and Dr. Biggs, that the bacilli were found inside of the giant cells. One might be led to suppose that here also the giant cell had had a phagocytic action. The cursory examination that he had made of the specimen presented by Dr. Valadier, hardly allowed of the expression of a definite opinion, but he was in doubt as to the presence of true pseudopods. The empty space around the cells was probably due to the hardening process to which the tissue had been subjected. He would be inclined to assume that the form of the cell depended upon the contraction resulting from the dehydration of those cells.

Dr VALADIER said that it had been suggested to him that these spaces might have resulted in the way just mentioned by the last speaker. If this were so, the sarcoma cells should not follow the same outline—the dehydration would hardly have the same effect on the cells and on the tumor.

The PRESIDENT said that the giant cells of sarcoma, syphilis, and tuberculosis had a different origin. The last two were the result of a necrobiotic process, as Dr. Waldstein had said. In 1887, the tubercle bacilli had been described in the interior of the giant cells of tuberculosis, and at this time a phagocytocic action had been attributed to these cells, but it had seemed to him quite as likely that the giant cell resulted from the massing together of a number of the epithelioid cells of a tubercle. These giant cells were formed at the point where the poison producing cheesy degeneration was most abundant. These became fused together, there was a drawing in of the nearest epithelioid cells to the mass, which gradually underwent a similar degeneration, and so the giant cell spread. In this way might be explained: (1) The frequent occurrence of tubercle bacilli in the centres of giant cells: (2) that the cheesy matter was usually in the centre of the giant cells in tuberculosis; and (3) the peripheral arrangement of the nuclei. There did not seem to be any doubt that the giant cells in tuberculosis were derived from the epithelioid cells, and not from any chance leucocytes. Another point strengthening this idea was the distribution of the nuclei at one end of the giant cell. In the sarcomata, the matter was totally different; it was strikingly suggestive of the myelo-plaques of bone marrow, and of the osteoclast. Moreover, we found these cells almost without exception in those sarcomata which had their origin in bone. If the giant cell in this form of sarcoma were the analogue of the osteoclast, then we might very properly attribute to it a phagocytic action. What the function of the myelo-plaques were, he did not know.

Dr. WALDSTEIN thought they were always found where calcareous matter had been destroyed, so that it was after all somewhat analogous to the other form of degeneration already referred to. The typical giant cell did not always have the nuclei at one end—they might be around the entire periphery, and in many cases it was possible to

demonstrate that the giant cell did not originate in epithelioid cells alone, even in tuberculosis, but from epithelial cells.

ABSCESS OF KIDNEY; CYSTITIS WITHOUT SYMPTOMS.

Dr. MARTHA WOLLSTEIN presented specimens taken from a married woman, twenty-nine years of age, who had been a patient in the New York Infirmary for Women and Children. The woman had had two children. The first symptoms of her last illness developed one week after the second confinement, and four months before her death. After exposure to cold, the feet and ankles began to swell, and one week later, anorexia, diarrhœa, and vomiting were present. The œdema then spread very rapidly, and soon culminated in a general anasarca. After three weeks of treatment in the hospital, the œdema all disappeared. The youngest child died shortly after this, and the mother's symptoms almost immediately returned, probably as a result of exposure to cold. There were symptoms indicative of pneumonia—a temperature of 101° F., respirations 36, pulse, 120—although during the month she was in the Infirmary the temperature did not exceed 100° F. The œdema was the most marked symptom, and was quite general. There was fluid in the peritoneal and pleural cavities. The urine was pale, had a specific gravity of 1018, and contained much albumen, some leucocytes, with epithelial and granular casts. There was no uræmia. At the autopsy, it was found that the pleural cavities contained about three pints of fluid. There was no pleurisy; some red hepatization in the right lower lobe, and marked œdema of both. the heart was practically normal. There was a typical nutmeg liver. A large quantity of fluid was found in the peritoneal cavity. The spleen was soft, friable, and congested. The stomach and intestines were normal. The right kidney showed the typical appearance of the large white kidney. In the upper part was a depressed, yellowish cicatrix, measuring about half an inch. The left kidney was very adherent, and it was much smaller than the

right. Only about one-third of the organ was true kidney tissue, the remaining portion having been converted into cheesy matter. This was stained for tubercle bacilli, but none found. Both ureters were patent. The bladder showed chronic cystitis, especially around the trigone. The uterus was normal, and in a state of hyper-involution. The tubes and ovaries were normal.

The interesting points in the case were: (1) The absence of symptoms of cystitis throughout the entire illness; (2) the relative age of the lesions; and (3) the absolute age of both lesions.

Dr. MARY PUTNAM JACOBI said that in view of the cystitis it was possible that the abscess of the kidney might have been due to an ascending process from the bladder, prior to the last confinement. She thought that this was the case, and that it explained why the overworked right kidney had been so susceptible to cold. It was unfortunate that no examination of the ureters had been made during life. The absence of pus in the urine would seem to show that nothing had been discharged from the left kidney for a long time.

ENDOTHELIOMATA OR EPITHELIOMATA OF THE NECK.

Dr. GEORGE P. BIGGS presented specimens taken from a man, seventy years of age, who five months before coming under observation, had first noticed a small lump beneath the right side of the lower jaw. This had grown steadily, but had caused no pain until a few weeks before coming under observation. Another lump had developed at a corresponding point on the opposite side of the neck a few days before his admission. Both tumors were removed. The first one measured 5 by 4 by 3½ ctm.; the second, 4 by 3 by 2½ ctm. That on the right side had recently caused some ulceration of the skin. Both tumors were circumscribed, but not distinctly encapsulated. Attached to each one of the tumors was some submaxillary gland tissue. Both tumors were quite firm, and, on section, presented a grayish, granular appearance, with scattered yellowish points. They

resembled in gross appearance rather an epitheliomatous growth than a connective-tissue growth. The gross and microscopical appearances of these tumors and the one next to be presented were the same.

Specimens were also presented from a man, forty-six years of age, who, eight months prior to coming under observation, had first noticed a small growth on the right side of the neck, near the angle of the jaw. This had grown steadily in size until, on admission, it extended from the thyroid cartilage in front to the posterior border of the sterno-mastoid muscle behind, and from the cricoid cartilage below up to a point behind the lower jaw. It completely surrounded the internal jugular vein, so that a portion of this vein was resected at the operation. The mass measured 5 by 5 by 2½ ctm., and was accompanied by several enlarged lymphatic glands. In these were circumscribed areas of distinct tumor tissue. Microscopically, all these tumors presented circumscribed areas of cells, which appeared to have developed in some pre-existing channels. The cells were arranged in concentric layers, those most central being large and epithelioid in appearance, while the middle and outer layers were smaller and ovoid. At the periphery of the lobules a regular row of cells formed a sharp outline. A few very small pearl-like bodies such as occur in endotheliomata were seen. In the central portion the cells were more or less degenerated. He was disposed to consider these growths identical with several recently described as endotheliomata, but he would like an expression of opinion on this point.

SUBMAXILLARY TUMOR—MUCOID DEGENERATION.

Dr. BIGGS also presented a tumor removed from a boy, fourteen years of age, who had first noticed the growth under the angle of the jaw, two years and a half before coming under observation. It was situated very close to, but was apparently not connected with, the parotid gland. It measured 3 by 2 by 1 ctm., and was irregular in outline. Some portions appeared to consist entirely of viscid, transparent

mucus. Microscopical examination showed that a considerable proportion of the tumor had undergone mucoid degeneration, but in certain parts were ovoid spaces, lined and filled with cells which were of epithelial type and not much degenerated. It was impossible to determine the origin of the tumor, but possible sources seemed to be an outlying portion of parotid gland or one of the fœtal ducts of the neck.

Dr. THACHER said that the specimens presented by Dr. Biggs reminded him of a dermoid cyst over the coccyx which he had examined. The lining wall of the cyst had been made up of cells having a very similar size and shape. He thought that the tumor presented might be an endothelioma of branchial origin.

The PRESIDENT said that possibly the last tumor presented might have been a portion of the parotid gland, which had become entirely separated from the main portion of the gland, and had become converted into a retention cyst.

Stated Meeting, Nov. 11, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

TUBERCULOSIS.

Dr. ROWLAND G. FREEMAN presented specimens from a colored child, three years and a half old, who died at the New York Foundling Asylum on April 25, 1896. A short time previously the child had had measles and pneumonia. There had been scattered râles over the chest; the spleen could be felt, and there was one enlarged lymph node on the right side of the neck. The clinical diagnosis had been tuberculosis. The autopsy had been performed immediately after death, and on opening the thorax a large mass of enlarged lymph nodes had been found in the anterior mediastinum, and also a line of enlarged lymph nodes on the upper surface of the diaphragm. The largest ones were two inches in diameter. In some places they were hard, in others

there was miliary infiltration. The lungs were bound down by adhesions, and contained very moderate amount of tuberculous infiltration. The bronchial nodes were much enlarged, and of the same character as those in the anterior mediastinum and along the diaphragm. The omentum showed very beautiful miliary tubercles. The capsule of the liver was studded with white tubercles, about one-sixteenth of an inch in diameter. The spleen showed the same appearance on the surface. The kidneys were pale. The mesenteric nodes just below the liver were enlarged. Adjacent to the caput coli was a node, half an inch in diameter, and over this the mucous membrane presented an ulcer about one-fourth of an inch in diameter. It was probable that this was the origin of the infection.

Dr. HENRY POWER said that the case presented had suggested the question as to whether the tubercle bacilli could pass through the stomach without being destroyed. It seemed to him that they would not necessarily be destroyed on account of the protection afforded by the mucus.

Dr. FREEMAN said that he thought there was exceedingly good authority for believing that the tubercle bacilli were not destroyed in the stomach. Experiments had been made in this direction with artificial gastric juice, and also on animals, and these indicated that the bacilli were not destroyed. He had presented quite a similar specimen to the Pediatric Section of the Academy of Medicine last spring.

Dr. WILLIAM VISSMAN did not think that tubercle bacilli could pass through the perfectly healthy stomach and retain their vitality; however, as the stomach was rarely entirely healthy, it was probable that the tubercle bacilli often passed through safely. An argument in favor of this view was the occurrence of more extensive lesions above than below the stomach. He recalled the case of a young lady, a member of a markedly phthisical family, in which both tuberculous peritonitis and enteritis occurred, yet there was no cough.

The PRESIDENT thought there could be little question that tubercle bacilli often passed the stomach in a perfectly viable condition. This bacillus was known to be rather resistant to external influence, such as drying, and the slight exposure to the acid gastric juice would hardly seem sufficient to kill them. Tuberculosis had been very frequently produced experimentally by feeding animals with the tubercle bacilli. Again, as Dr. Vissman had said, the stomach in consumptives was frequently deranged, and the degree of acidity lessened. He found it rather hard to believe that the very small ulcer in the caput coli, in the case presented, was the point of entrance of the large number of tubercle bacilli that must have been disseminated through this child's body in order to produce such extensive lesions in the glands. The ulcer appeared insignificant, there was but little infiltration in the wall of the intestine about it, and he was inclined to think that the ulceration was of recent development, quite possibly as a result of the extension of the process from the lymph nodes. He did not mean to say, however, that the case was not one of intestinal infection, for the evidence pointed strongly to such an origin; yet he felt that the bacilli were so generally inhaled in cases of tuberculosis in which the bronchial lymph nodes were so much enlarged, that it was not at all unlikely that in this case both modes of infection had been in use.

Dr. FREEMAN said that in tuberculosis the main lesion was often found at a considerable distance from the point of entrance. Thus, in tuberculous meningitis, a very considerable meningitis might be present, and yet no other marked lesion elsewhere could be detected.

Dr. F. M. JEFFRIES presented specimens from a case of

GENERAL TUBERCULOSIS.

The patient was forty-four years of age, and died two days ago. There were small nodules over the pericardium. The pleural cavity was entirely obliterated, and the pleura

contained small tubercles. In the liver were to be found here and there very small nodules, apparently tuberculous, but difficult of detection.

Dr. JEFFRIES also exhibited the lungs from another case of tuberculosis. In the upper lobes were cavities, and nodules were scattered throughout the organ. No clinical diagnosis of tuberculosis had been made, notwithstanding the advanced stage of the disease.

Dr. JEFFRIES also presented specimens taken from a woman who had been for two days in the alcoholic wards at Bellevue Hospital. On admission, her temperature had been 100° F., but it had gradually risen, until just before death it had reached 104° F. No complete physical examination had been made. The autopsy showed marked general tuberculosis. The peritoneum was studded with tubercles; the diaphragm was adherent to the liver; the liver was enlarged and fatty; the kidneys showed tubercles, both in the cortex and in the pyramids. The supra-renal bodies were apparently not affected. All of the glands around the pancreas were greatly enlarged, and apparently cheesy. The lungs were the seat of what appeared to be acute tuberculosis. There were a few tubercles in the spleen.

PHOTOMICROGRAPHS OF BACTERIA.

Dr. HENRY POWER exhibited a photomicrograph taken with an amplification of 2500 diameters, and showing the absence of the usual halo. He said that in looking at bacteria with a very high power, it was often difficult to determine whether or not a capsule was really present. This appearance, he believed, was due to a particular mode of illumination. His theory was that the appearance was produced by the bacteria having a high refractive index and acting as a lens. Acting upon this theory, he had used Dr. Piffard's new mounting medium, and had found that this lens-action had been destroyed, and the difficulty alluded to had been completely obviated.

TUBERCULOSIS OF THE GUM.

Dr. J. S. ELY presented microscopical specimens of a case of tuberculosis of the gum. He said that this condition was rather an unusual one, or at least was not often recognized. The material from which the specimens had been prepared, had been sent to him by Dr. R. H. M. Dawbarn for examination. The lesion had occurred in a young man who had been apparently perfectly healthy, with the exception of a slight ulceration in the mouth on the side opposite to that at which the lesion had developed later. The ulceration had been treated with dilute acid. A portion of the tissue had been submitted to him for microscopical examination, and he had found unmistakable evidence of tuberculosis. Dr. Dawbarn had since incised and scraped the part thoroughly, and the report was that at the present time the parts were apparently healing. Dr. Ely said that he had been able to find only one case of tuberculosis of the gum on record, and this had been reported by a Swede, in 1884. The case had been reviewed in Virchow's *Jahresbericht*. The patient, who was forty years of age, had severe pain in the mouth and radiating towards the left ear. On examination, an ulcer with undermined edges was found behind the lower left wisdom tooth, and extending to the fauces, and later on to the soft palate. The base bled readily. At the same time, small grayish nodules were found scattered over the pillars of the fauces and over the soft palate. These nodules subsequently increased in size, and finally became confluent ulcers. The microscopical examination had left no doubt whatever as to the tuberculous nature of the growth, and tubercle bacilli had also been found in the tissues, and in a cavity of a wisdom tooth which was extracted. The patient ultimately died of tuberculosis.

Dr. Ely said that this case had led him to study the subject of tuberculosis of the mouth, and he had been able to find but few cases on record. Attention had been first called

to this condition by Ricord prior to 1872. In 1872, a case of three tuberculous ulcers on the right edge of the tongue was reported by Reverdin, in a man, forty-six years of age, suffering from phthisis. In 1883, two cases had been reported. In one of these there was an ulcer of the lower lip, and in the other an ulcer of the tongue. Tubercle bacilli were found in both cases. There was also on record a case of "tuberculous angina," occurring in a phthisical patient, in which there were grayish ulcerating patches on the anterior pillars of the fauces and soft palate. The ulcers had undermined and indurated edges, and microsopical examination proved them to be tuberculous. He had found on record a case of lupus of the pharynx, and in 1887, at the Heidelberg clinic twelve cases had been reported of lesions in different parts of the mouth, but principally upon the tongue and lips. In two of the cases, the lesion in the mouth was the only tuberculous lesion that could be detected, so that undoubtedly a lesion might exist as a purely local one, and be amenable to treatment. In about half of his cases he had succeeded in healing the ulcers, In 1887 Dr. Delavan had reported a case of tuberculosis of the tongue, and later, Dr. Bull had published a report of the surgical treatment of that case by amputation of the tongue. There had been no recurrence in this instance.

Dr. W. H. PARK remarked that in a large dispensary practice in throat diseases he had not come across a single case of tuberculosis of the gum. Such lesions in the pharynx were, however, fairly frequent.

Dr. ELY said that in studying the literature of the subject, he had observed that the salivary glands seemed to be quite frequently affected.

Dr. F. M. JEFFRIES exhibited a specimen of

EXTRA-UTERINE PREGNANCY.

He said that on examination nothing had been found but bloody fluid, the fœtus having been macerated, but sections from the walls showed placental tissue.

ATROPHY OF LEFT LOBE OF THE LIVER.

Dr. JEFFRIES also exhibited a liver showing almost complete atrophy of the left lobe. The liver had been removed from a man of forty years. There were no other features of interest at the autopsy.

RUPTURE OF ANEURISM INTO PERICARDIUM.

Dr. JEFFRIES then presented specimens from a case of sudden death, due to hemorrhage into the pericardial sac from the rupture of a small aneurism of the arch of the aorta.

Dr. MARTHA WOLLSTEIN reported that examination of the specimens presented by her at the last meeting showed them to be non-tuberculous, and that the case was one of ordinary chronic cystitis with an ascending nephritis.

The Society then went into executive session.

Stated Meeting, November 25, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

BACILLUS AEROGENES CAPSULATUS.

Dr. JAMES EWING presented specimens from a fatal case of placenta prævia, occurring at the Sloane Maternity Hospital. *Accouchement forcé* had been done for a median placenta prævia, and immediately after the operation, and again two hours later, a considerable quantity of salt solution had been infused. She died four hours after delivery, apparently from acute anæmia and shock. The autopsy was made within fifteen hours after death. There were no signs of cadaveric decomposition, but the anæmia was extreme. There was an entire absence of rigor mortis. In the region of the uterus, on the right side was a considerable extravasa-

tion of blood in the broad ligament, and the tissues in this region were very emphysematous. There was a less degree of emphysema on the left side. The spleen was enveloped in what appeared to be a loose membrane, but which proved later to be its capsule which had been distended by the gas or air found in the region of the right broad ligament. The capsule was almost stripped off from the spleen. The surface of the liver showed a considerable number of small air vesicles. On section, there was distinct crepitation. The kidneys showed slight acute degeneration, and in a few places, these same air vesicles or blebs. On opening the heart, it was noted that no air escaped, and no lesions were found except just below the aortic valves, where the endocardium was slightly stripped from the myocardium by exceedingly minute air blebs. The vessels in the neighborhood of the uterus were slit up as far as the inferior vena cava. All of these vessels contained frothy blood. The vessels in the neighborhood of the site of the injection were free from air. The cause of death was undoubtedly the acute anæmia. The chief point of interest was the development of this quantity of gas in the course of a very few hours. From the quantity of air present, it seemed as if air embolus could be fairly excluded, and that the condition was probably due to the *bacillus aërogenes capsulatus*. Dr. Norris had succeeded in isolating this bacillus and growing it.

The speaker said that this subject was now exciting considerable attention. It had been admirably condensed in an article by Dr. Welch in the first number of the *Journal of Experimental Medicine*. Welch had first published the observations on this bacillus in the *Johns Hopkins Bulletin* for 1893, but Fraenkel, independently of Welch, had identified a similar bacillus as the cause of malignant œdema. Welch stated that the bacillus had been undoubtedly seen again and again before he discovered or isolated it, but he had found no record of such a discovery. In 1889, Dr. R. G. Freeman had presented to this Society a case in which the bacteriological examination had been made by Dr. Prud-

den. The growth had been attempted on gelatin, but had proved negative. In sections of the liver, which were distended with these air blebs, he had found large masses of a bacillus corresponding with the description given by Welch. It was not known at that time that the bacillus was an anaërobic. Not long after the publication of the articles of Welch and Fraenkel, it was found that this germ could be found during life, as well as post mortem. Fraenkel, in 1893, isolated it from gaseous phlegmon, and about this time a case had been reported in which a patient died of acute septicæmia after an abortion, and all the tissues had been found extremely emphysematous. From this a pure culture had been obtained of the *bacillus aërogenes capsulatus*. Welch had seen several cases of bullet wounds and railroad crushing injuries in which, in from sixteen to twenty-four hours after the injury, the patient had been affected with the usual symptoms of septicæmia, but associated with the development of gas. These cases had usually proved fatal. He mentioned six cases of gaseous phlegmon, one of fibropurulent peritonitis due to rupture of an ovarian cyst, two of peritonitis due to rupture of typhoid ulcers, and two cases of pneumo-peritonitis from typhoid fever, without rupture of the intestine, thus indicating that the bacillus could travel through the unbroken peritoneum. Another case, reported by Welch, followed a strangulated hernia, and another a hemorrhagic infarction of the intestine. It had been found in pleurisy where there was no possibility of infection from without, and it had been known to follow infarction of the lung, and to occur in one case after pneumonia. These cases showed that the bacillus in question had a very wide distribution, and might, therefore, complicate any ordinary case of septicæmia.

Dr. CHARLES NORRIS presented a number of culture tubes showing the growth of the *bacillus aërogenes capsulatus*, and also exhibited under the microscope a smear made from the liver. One of the cultures had been made on an agar plate in an atmosphere of hydrogen for three days It

exhibited the typical colony with the branching processes from the borders.

The PRESIDENT said that these were the first cultures of this germ that had been made in this city. He asked if there were any association of this germ with the subcutaneous emphysema sometimes noticed—a condition often transitory. The condition was apparently not inflammatory. He recalled seeing in Bellevue Hospital such a case. In this case, there was a sudden development of an emphysema in an individual, appearing first in the groin and abdomen, and then extending down nearly to the knee. After about twenty-four hours it disappeared without having given the patient any special inconvenience.

Dr. EWING replied that he had never seen such a case. The introduction of this bacillus into the human system was always marked by fever and other marked constitutional disturbance. He desired to emphasize the fact that the three cases observed at the laboratory of the College of Physicians and Surgeons had been in connection with parturition and operations on the uterus. In two of these there had been very severe hemorrhage. The growth of the germ is extremely rapid, for when the liver was removed it contained only a few vesicles, yet within one hour the air vesicles were large and very numerous. The medico-legal bearing of this subject should be mentioned. Welch had called attention to the importance of making a bacteriological examination to determine the presence or absence of this bacillus in cases of supposed air embolus. Air embolus had always stood as a diagnosis in medico-legal works, yet Welch thought it probable that many of these cases had been really infections with the *bacillus aërogenes capsulatus*.

CHONDROMA OF THE FINGER.

Dr. J. S. ELY presented two tumors of the hand. The first one presented was a chondroma removed from the left little finger at the metacarpo-phalangeal articulation. The

patient, a man, twenty-three years of age, had noticed a small lump about ten years prior to the removal of the tumor, at a right metacarpo-phalangeal articulation. Similar tumors developed at all of the joints of the little finger and ring-finger of the right hand, and later at one metacarpo-phalangeal joint on the left hand—in other words, the tumor presented was the last one to develop. These tumors were quite large, but were painless, and did not interfere with the movements of the fingers. He would only consent to the removal of the tumor on the left hand. This tumor measured about 3 by $2\frac{1}{2}$ ctm. The section presented showed the typical structure of a chondroma. This structure was interesting as illustrating the extreme lawlessness of tumor growths in general.

RECURRENT GIANT-CELL SARCOMA OF THE HAND.

Dr. ELY then exhibited a recurrent giant-cell sarcoma of the hand. He said that on January 1, 1896, Dr. Dawbarn had brought to him a tumor for examination, which had been removed from a man of twenty-five years. The specimen was the fourth finger of the left hand, the third and fourth metacarpal bones and surrounding tissues, and a small tumor situated at the end of the third metacarpal bone in the tissues between it and the base of the fourth finger The tumor was spheroidal, and measured 3 by 3 by 2 ctm. It was quite freely movable and rather hard. No attachment to adjacent metacarpal bones could be made out. On section, it was fleshy in appearance, lobulated, and rather sharply circumscribed. This tumor was a recurrent growth, the third finger having been removed about six months before. Microscopical examination of the recurrent tumor showed it to consist for the most part of spindle cells closely packed together and lying in the meshes of a fine reticulum of fibres, scattered through which were many giant cells of variable size and shape. There was no sign of degenerative change in any part of the tumor.

The first tumor removed was a finger greatly enlarged and almost destroyed at its base.

From a study of this last specimen he thought there was but little doubt that the giant cell sarcoma originated in the proximal phalanx of the finger, and probably from its periosteum. A rather interesting feature in this case was that there was absolutely no involvement of the skin. The tumor had grown from the remnant left at the first operation. The healing of the wound was perfect, and there was no subsequent breaking down of the cicatrix as was so often the case with recurrent sarcomata. Ziegler considers the hand the most frequent site of chondromata in general. An examination of the recurrent tumor seemed to indicate that there was no liability of its recurrence again unless there had been a metastasis prior to this last operation. He did not consider such a tumor very malignant.

Dr. EWING recalled a tumor of similar appearance in a similar situation. It had been removed in a not very radical manner, and there had been a recurrence in a short time. Just before a second operation had been contemplated, the tumor had begun to disappear, and had ultimately been entirely absorbed. There had been no further recurrence. He would like to ask Dr. Ely if he considered these giant cells to be derived from the osteoclasts.

Dr. ELY replied in the affirmative. He said that if a tumor were not sharply circumscribed one was justified in attributing to it a more malignant character than to a distinctly encapsulated tumor like the one just presented. Even in the worst cases, giant-cell sarcoma was not so malignant as a melano-sarcoma. He thought that giant-cell sarcomata were quite frequently encapsulated. These tumors usually destroyed bone very rapidly, yet he did not recall ever having seen a distinct metastasis from a giant-cell sarcoma.

The Society then adjourned.

Stated Meeting, December 9, 1896.

JOHN SLADE ELY, M. D., PRESIDENT.

THE FORMATION OF GIANT CELLS.

Dr. ANNA W. WILLIAMS exhibited under the microscope a number of sections from the lung of a child. These were obtained from a laboratory jar, labelled "miliary tuberculosis in a child," and no history bearing on the condition was available. There were two pieces of lung—one from the neighborhood of the hilus, showing consolidation on gross examination; and the other, taken from the apex, showing a few scattered miliary tubercles. The sections exhibited were from the first portion. From the appearance of some of the giant cells, the speaker said, she had been led to conclude that their mode of formation was more complicated than was generally supposed. The sections had been stained for tubercle bacilli, with positive results, and serial sections had been stained with hæmatoxylin and eosin. Under a low power, a large number of giant cells are visible, many of them circular or oval, having an unusually regular outline, suggesting a wall, and the nuclei arranged more or less regularly about the periphery within this wall. Other cells are more irregular, and less well defined. These cells are generally the centre of a small group of epithelioid cells. Under a high power, the "wall" is found to be composed of elongated cells, with oval nuclei such as one sees in cross-sections of small blood- or lymph-vessels. Within this wall are more oval nuclei, and some spheroidal cells. The centre shows a granular and more or less homogeneous mass. The serial sections show that many of these giant cells are much elongated and branched. The branches are narrow and oblong, bounded by elongated nuclei, giving the appearance of a small vessel. The blood-vessels in these sections show little change except that the smaller ones in the vicinity of the tubercles have their walls infiltrated with small spheroidal

cells. The bronchi show the changes of simple exudative inflammation.

From these specimens it would seem reasonable to conclude that the principal infection occurs through the lymph-channels; that the lymphocytes taking up the tubercle bacilli and becoming agglutinated and degenerated, small particles of these degenerated masses pass to the smaller lymphatics, plugging them, and causing a thrombus. The lymphocytes collect about the periphery of the vessel at this point, the endothelial cells increase, and necrosis extends from the centre. The observations made by Borrel on the formation of the giant cell in tuberculosis, as published in his article, "Tuberculose Pulmonaire Experimentale" (*Annales de L'Institute Pasteur*, 1893), were interesting in this connection. He inoculated a pure culture of tubercle bacilli into the ear-vein of rabbits, killing an animal immediately after the inoculation, and others in ten minutes, thirty minutes, three hours, fourteen hours, and then every twenty-four hours. Sections of the hardened lungs were studied. He found that immediately after the inoculation there developed an intense polynuclear leucocytosis, most of the leucocytes containing bacilli. After a day this general polynuclear leucocytosis disappeared, and only a varying number of groups of these leucocytes containing bacilli remained in the blood-vessels. The evident decrease in the number of leucocytes was due to the fact that the blood stream carried some of them to other parts of the body, while others passed through the vessel wall into the alveoli of the lungs. On the third day the leucocytes containing bacilli in the blood-vessels showed degenerative changes, gradually breaking up, and setting the bacilli free. As this last change was going on, a number of large mononuclear leucocytes formed about the periphery of the vessel at the place where the degenerated polynuclear leucocytes were grouped, enclosing the degenerated elements. Through the fusion of these mononuclear leucocytes with the central detritus, giant cells were formed. These Borrel called the intravascular giant cells.

He did not say that he observed an increase in the connective-tissue cells of the blood-vessel wall, but that this takes place was very probable, especially when there are few bacilli, or when they are less virulent, or the individual predisposition to tuberculous infection was not great. In the present case only a few tubercle bacilli were found, and these were at the periphery of the more degenerated giant cells.

Dr. HENRY POWER said that he thought some of the appearances would lead to the conclusion stated by Dr. Williams regarding the formation of the giant cells. Such a conclusion could not be made positively, however, without more prolonged study of the specimens.

The PRESIDENT said that the specimens certainly indicated that some of the giant cells were formed in the manner claimed. In the cross-sections many of the giant cells could be followed for a considerable distance, and with that regularity which would be observed if they had been formed in a channel. He saw no reason why giant cells should not be formed in this way.

Dr. POWER asked what prevented the larger lymphatics from taking part in the same change.

The PRESIDENT replied that to get such a formation the lympathic to be occluded must be rather small. If a small bit of cheesy matter should happen to gain lodgement, the arrangement would be eccentric. One would hardly expect that a large particle would be carried along in this way.

Dr. JAMES EWING presented specimens hardened in alcohol from a case in which death occurred from chloroform narcosis. In connection with this case, he made some remarks on:

THE LYMPHATIC CONSTITUTION, AND ITS RELATION TO SOME FORMS OF SUDDEN DEATH.

Under the term *constitutio lymphatica* have rather recently been described a series of cases presenting a characteristic hyperplasia of the lymph nodes, spleen, thymus, and often

of the lymphoid marrow, associated with hypoplasia of the heart and aorta, and frequently also with rhachitis. These pathological conditions have been found especially in cases of sudden death, from a variety of causes, and are believed by many to indicate in these subjects diminished vital resistance and special liability to sudden cardiac paralysis.

The importance of the *constitutio lymphatica* and its relation to some forms of sudden death, especially to fatalities under chloroform narcosis, have been recognized for several years by the Vienna school of pathologists, but have received very scant attention elsewhere.

Two cases of sudden or unexpected death which have recently come to the writer's hands have shown in a striking degree some of the characteristic anatomical features of the lymphatic constitution, and seem to furnish rather convincing evidence of the correctness of the views recently advanced in regard to this condition.

In addition to the report of these cases, the writer has endeavored to briefly review the evidence on which are based the present views on the subject, and further, to consider in some detail the separate features of the lymphatic constitution and their pathological aspect in this and other conditions.

CASE I.—E. F., a girl, aged five years. Parentage, Irish.

Family History.—No relatives were known to have suffered from tuberculosis, enlargement of lymph nodes, tumors, or from any tendency to hemorrhages or anæmia. Several immediate relatives died of nephritis, rheumatism, and endocarditis. Father and mother have always been healthy. A brother, two years old, was carefully examined on account of a possible reproduction of some of the conditions seen in the sister. This child looked well. All superficial epiphyses seemed normal, and there were no signs of rhachitis other than a markedly protuberant abdomen. The cervical lymph nodes were distinctly palpable from the angle of the jaw to the clavicle. In one axilla a considerably enlarged node was detected. The inguinal nodes were of moderate size and

not distinctly enlarged. The epitrochlear nodes could not be felt. The tonsils were moderately enlarged, but not hyperæmic, being identical in appearance with those found at autopsy in the sister. The child always breathed through the nose. The thyroid was not enlarged; the thymus could not be detected; the area of splenic dulness was not enlarged, although distinct.

Examination of the blood showed the red cells to be normal. There was a moderate increase of leucocytes, of 500 of which 76 per cent. were uninuclear, mostly small or medium-sized lymphocytes, 22 per cent. multinuclear, 2 per cent. eosinophile. No normoblasts were seen.

The examination of this child indicated therefore, indistinctly, a constitutional tendency similar to that demonstrated at autopsy in the sister. That the child is really a subject of the lymphatic constitution it is not intended to state, but that a series of such examinations would be a desirable addition to our knowledge it is hardly necessary to urge.

A baby brother of four months appeared perfectly healthy.

Previous Personal History.—The child had always been regarded as healthy. At two years and a half had had measles, the attack being of moderate severity. Three months before her death she had a mild attack of scarlatina, while the younger brother was passing through a very severe attack. The appetite was always good, and there were no previous gastro-intestinal, pulmonary, or renal symptoms, except a tendency to constipation.

On October 5th the patient fell by accident in the street and received an incised wound of the tongue, which had been caught between the teeth. The bleeding from the wound continued for an hour and alarmed the mother, who brought the child, pale and frightened, to the Roosevelt Hospital, out-patient department.

The further history of the case was furnished through the kindness of Dr. Zerega. Chloroform was administered in order to place a few sutures in the wound, which was still

bleeding moderately. The anæsthesia proceeded uneventfully for fifteen to twenty minutes. The inhalations had been interrupted once to allow the stitching to proceed. The child had partly regained consciousness and the inhalations were again begun, when it was noticed that the face was very pale, and the pulse, previously good, was impalpable. Vigorous attempts at resuscitation, including tracheotomy and artificial respiration, were without effect. The pulse never returned, the breathing failed steadily, and, although feeble gasps were elicited at intervals for half an hour, respiration finally ceased entirely, and the child was pronounced dead.

Autopsy (*twenty hours after death*).—Body well nourished, without rigor. Post-mortem lividity faint, the skin being generally pale. Heart: Size normal, walls flaccid, left ventricle contains an ounce of dark fluid blood. Right chambers moderately filled with dark fluid blood. Endocardium normal. A few subpericardial ecchymoses. Aorta of normal size. Lungs: Blood contents considerable. There are numerous subpleural ecchymoses. Bronchi: Beginning suddenly an inch below the cricoid cartilage—that is, at the level of the tracheotomy wound—the bronchi are deeply reddened. No foreign matter in trachea or bronchi. Mucous membrane of larynx and epiglottis slightly shrunken. Liver contains much fluid dark blood. Thymus measures $7 \times 5 \times 2$ centimetres, and covers the upper third of pericardium. Spleen slightly enlarged. Malpighian bodies extremely prominent, looking like large miliary tubercles. Pulp very hyperæmic. Stomach: The solitary follicles, especially about the pyloric end, are distinctly visible. Intestine: Throughout the entire intestinal tract, especially in the ileum, the solitary follicles are very prominent. Peyer's patches are enormously hypertrophic. The lower lenticular patches measure eleven to nine centimetres in length, and the enlarged nodules of the lowermost patch appear as distinct polypoid outgrowths half a centimetre high. The mesenteric nodes are all very much hypertrophied, forming

a solid mass of lymphoid tissue, in which the outlines of the individual nodes are intact, while the separate superficial nodules are distinctly visible through the capsules. The mass of these nodes appear quite large enough to have been palpated through the abdominal wall. The faucial tonsils are moderately enlarged, but not hyperæmic. The lingual tonsils are moderately enlarged. The axillary and cervical lymph nodes are slightly enlarged. The bronchial nodes appear normal in size. The bone marrow was not examined. There are no evidences of rhachitis in the ribs, skull, or superficial epiphyses. The brain appears normal. The pia is congested and slightly œdematous. The choroid plexuses are intensely congested. The examination of the blood of a small pial vein shows the red cells to be normal in appearance. Of five hundred leucocytes, 84 per cent. are uninuclear, and of small or medium size, 16 per cent. are multinuclear, and no eosins were found.

The autopsy indicated, therefore, death by asphyxia, as shown by the dark color and fluidity of the blood, the general venous congestion of the viscera, and the subpericardial and subpleural ecchymoses.

Microscopical Examination.—Spleen: The densely packed masses of lymphoid cells of the Malpighian bodies were usually sharply marked off from the pulp tissue, but in some instances the surrounding pulp tissue was infiltrated for some distance with a considerable number of lymphoid cells. Some of the Malpighian bodies consisted of two symmetrical portions surrounding separate small adjoining arteries, and often in these cases one portion of the follicle consisted of the very densely packed masses of lymphoid cells, while in the other portion the cells were not more numerous than in the normal spleen. A few small collections of lymphoid cells were scattered throughout the pulp tissue without connection with the Malpighian bodies.

The splenic sinuses were uniformly dilated and gorged with blood. There was a markedly increased deposit of pigment granules throughout the organ, approaching in

grade that of malaria or pernicious anæmia. This pigment appeared under three different conditions: (1) The sinuses contained many macrophages enclosing many fine, brownish-black pigment grains, most abundant about the nuclei. (2) Lying free in the sinuses were many large, single or conglomerate, yellowish, translucent granules of about the size of red blood-cells. (3) Conglomerate masses of black granular pigment were occasionally seen lying free in the sinuses. Potassium ferrocyanide and acidified glycerin developed a moderate reaction of diffuse hæmosiderin. There were no evidences of interstitial splenitis.

In the polypoid masses of the Peyer's patches the follicles were much increased in number, the proliferation zones were very distinct, and a very few outlying small collections of lymphoid cells were found close to the muscularis. There was an entire absence of pigment in the lymphoid follicles of the gastro-intestinal tract. The mesenteric lymph nodes showed uniformly the appearances of simple hyperplasia without inflammation.

The signs of the lymphatic constitution were, therefore, general hyperplasia of the lymphoid organs, including thymus, spleen, gastro-intestinal and mesenteric lymph nodes, the faucial and lingual tonsils, and the cervical and axillary lymph nodes. Hypoplasia of the heart and aorta was not present, and there were no evidences of rhachitis.

CASE II.—M. B., female, aged twenty-seven years, was brought to Sloane Maternity Hospital, January 31, 1896, suffering from shock and hemorrhage, due to attempts to deliver a full-term child through a contracted pelvis. A high forceps operation had been attempted unsuccessfully. Version had then been performed, and the child's body had been twisted from the head and extracted, leaving the head *in utero*. On admission the patient's pulse was 132, and she was extremely pallid, evidently having lost considerable blood.

The head was removed by cephalotripsy, and the adherent placenta was detached with the further loss of eleven ounces

of blood. Active stimulants were administered, with the result of improving the patient's condition considerably and reducing the pulse to 92, but she failed gradually, with symptoms of shock and hemorrhage, and died six hours after admission—fifteen hours after the beginning of labor.

Autopsy (*eight hours after death*).—Body of a moderately fat, rather large woman; skin pale; no œdema; slight rigor mortis. Heart is distinctly under normal size. Wall of left ventricle slightly hypertrophied. Valves normal. Aorta abnormally small, down to division of iliac branches. Lungs slightly congested. Liver: Consistence reduced, centres of lobules slightly reddened, peripheries very light colored. Kidneys: Size normal, capsule not adherent, markings slightly irregular, but distinct. Spleen soft, anæmic. Malpighian bodies indistinct. Gastro-intestinal tract normal. Uterus shows a linear tear of cervix, extending for three inches up through internal os and out into right broad ligament. Perinæum torn to sphincter ani. Pelvis: Sacrum is sunken downward and forward, diminishing antero-posterior diameter of pelvis, which measures nine centimetres, and widening the transverse diameter. Acetabula point forward: Superior strait is obstructed by forward projection of lumbar vertebræ, a deformity which is balanced by deficiency of vertebral bodies posteriorly and marked lordosis. The antero-posterior diameter of the chest is increased. The thymus is persistent, measuring $5 \times 3 \times 2$ centimetres. The lymph nodes are not enlarged. The blood content of the viscera and vessels is moderately diminished. The thyroid gland is considerably enlarged and its consistence somewhat firmer than is usual.

In this case the indications of the *constitutio lymphatica* consisted in the marked evidences of old rhachitis, the hypoplasia of the heart and aorta, and the persistence of the thymus.

It does not appear from the history that the patient showed any marked lack of vitality, and the case is reported rather to show the doubtful importance of some of the conditions

now believed to indicate the presence of the lymphatic constitution. It was, however, the opinion of the attending physicians that the patient's death was inadequately explained by the shock of the operations and the loss of blood, and the fatal termination was a matter of surprise, especially after the temporary improvement following the completion of the labor.

Consideration of the separate features of the constitutio lymphatica.—The observations which have resulted in the present views of the lymphatic constitution have been accumulating for a long series of years, and have had reference to a great variety of abnormal conditions or distinct diseases. The very wide scope of these observations, moreover, while largely reponsible for the present uncertainty as to the real limits of this term "lymphatic constitution," is yet strong *a priori* evidence that it represents an important fact in pathology.

These observations have been drawn from the study of chlorosis, leucæmia, pseudo-leucæmia, and hæmophilia in the province of the blood, of congenital hyperplasia and hypoplasia of various organs and tissues, of enlargement of the thyroid gland, with or without Basedow's disease, of enlargement of the thymus, of rhachitis, of the fatal effects of chloroform narcosis, and of the large class of cases of sudden death without organic lesions coming under the notice of medical jurists.

In all of the above conditions it has long been apparent that there was frequently associated a systemic weakness which, among other things, rendered the subject liable to sudden heart failure and death under a variety of apparently inadequate exciting causes.

The anatomical features which are at present believed to characterize the subjects of the lymphatic constitution include hypoplasia of the heart and aortic system of vessels, partial or general hyperplasia of the lymphatic organs, the spleen, thymus, lymph nodes, and the lymphoid or red marrow. There may also be evidences of rhachitis. The hy-

Photograph of the lowest Peyer's patch in Case I. Enlarged one third above natural size. (From photograph by Dr. E. Leaming.)

perplasia of the lymphatic structure of varying extent is the most constant and the essential characteristic, hypoplasia of the heart and aorta is frequently added, and evidences of rhachitis are present in the majority of instances. Enlargement of the thyroid appears so frequently in the reports of recent cases as to call attention to the possible importance in the morbid condition of changes in this organ.

Hypoplasia of the Heart and Aorta.—One of these conditions earliest studied is the hypoplasia of the heart and blood-vessels, first claimed by Virchow to be the fundamental pathological condition in chlorosis, and known to be frequently associated with certain other abnormalities in the blood and blood-vessels. The diminished vital resistance of such subjects and their liability to secondary organic dis eases were regularly noted by medical writers between 1860 and 1880, and special contributions, with illustrative cases, were made by various authors, such as Wunderlich, Riegel, Kulenkampff, and Kussner. More recently, Handford, Leyden, and Fraentzel have pointed out the frequent connection of arterial hypoplasia with cardiac disease.

Rokitansky, Virchow, Riegel, and Bruberger have reported cases of rupture of these imperfectly developed vessels.

Virchow's theory of the origin of chlorosis was supported and further extended to hæmophilia by the observations by Copeland and Bamberger of the coincidence of both of these diseases of the blood with congenital narrowing of the aorta. Otto and Rokitansky noted the frequency with which this anomaly was associated with hypoplasia of other tissues and organs. A case of this description has recently been reported by Israel. Recklinghausen found a general infantile grade of development in a woman of twenty-five years dying of acute phthisis, and showing in addition to hypoplasia of heart and aorta, a patent foramen ovale, a persistent thymus, lobulated kidneys, and infantile pelvis and sexual organs.

The diminished resistance of these subjects to infectious

diseases has been observed in cholera by Virchow, in pneumonia by Ortner, in typhoid fever by Fraentzel, Virchow, and Benecke. In two cases of sudden death during convalescence from typhoid fever, Hiller found uniform narrowing of the aorta. Ortner endeavors to explain the fatal course of some reported cases of anæmia after complete removal of the cause, the *Bothriocephalus latus*, by the coexistence of a narrow aorta and undeveloped sexual organs, which were found at autopsy in these cases.

Such miscellaneous observations might be multiplied at length, but sufficient evidence has been reviewed to show that hypoplasia of the heart and arteries, which is a prominent anatomical feature of the *constitutio lymphatica*, is often of itself an evidence of a congenital defect in physical development, and indicates a diminished vital resistance in the organism.

Whether cases presenting this anomaly alone should be classed with those showing more fully the features of the lymphatic constitution, the writer does not believe that the evidence at present available is sufficient to decide. For the present purpose it need only be claimed that the existence of this abnormity is in itself a probable ground for the belief that the subjects of the *constitutio lymphatica* possess inferior vital resistance.

Hyperplasia of the Lymphatic Organs.—The hyperplasia of the lymphatic structures of the body is a more recent contribution to the pathology of this form of diminished vital resistance, and the demonstration of its essential importance has served to correlate many facts previously known, and to justify the employment of the old term *constitutio lymphatica* revived by A. Paltauf for the general condition. That some underlying constitutional defect must be assumed to exist in order to account for many sudden deaths usually referred to the pressure of an enlarged thymus upon the trachea, bronchi, or great vessels, was the conclusion reached by Paltauf and others from a long experience with this class of cases at the Institut für gerichtliche Medicin in Vienna.

Since the time of Friedleben, who in 1858 denied that a normal or hypertrophic thymus gland could produce fatal laryngismus, there has been constant discussion of the manner of death in many cases of sudden death without apparent organic cause other than enlargement or persistence of the thymus, nor are opinions as yet in agreement on this subject. Many writers still claim that death in these cases is produced either by direct pressure of the enlarged thymus upon the bronchi or great vessels, or by reflex cardiac or respiratory paralysis arising from the thymus. Of such writers may be mentioned Recklinghausen, Nordmann, Gluck, Pott, Seydel, Grawitz, and Benecke, and their reported cases indicate that under some circumstances the pressure of an enlarged thymus may reach a dangerous degree. Only a small percentage of the deaths could, however, be explained on such a basis, as the patients usually died very suddenly and the hypertrophy of the thymus was often inconsiderable.

The observations of Paltauf convinced him that many of these fatalities, especially in infants, must be referred to a capillary bronchitis, of which the post-mortem evidences are often very meagre, and the observations of Paltauf, Hoffmann, and Kolisko have led them to believe that all the others are referable to a peculiar constitutional defect, of which an expression is to be found in general hyperplasia of the lymphatic structures. In the experience of these observers, the enlargement of the thymus in these cases is only one feature of a general lymphatic hyperplasia, involving also the spleen, the tonsillar ring, the thoracic and abdominal lymph nodes, and sometimes the bone marrow. Moreover, an examination of the cases of "*thymus Tod*" reported by earlier writers, even those of Friedleben, discloses the fact that in the majority of instances it was noted that the tonsils, spleen, and lymph nodes were more or less hypertrophic, although no particular significance was attached to this fact at the time.

The same observers noted a similar condition of general

hyperplasia of the lymphatic structure of the body in a series of sudden deaths during chloroform narcosis, and the study of these cases, which have recently been collected by R. Kundrat, together with the reports of similar cases from other sources, renders it possible to give a somewhat detailed description of the pathological changes in the enlarged organs, and of the other characteristics found at autopsy in these cases.

Pathological Changes in the Lymphatic Structures.—The thymus frequently measures from six to ten centimetres in length, reaching at times from the middle lobe of the thyroid to the heart's apex. Its consistence may be increased or it may be soft and exude on section a milky white fluid. It has been found adherent to the pericardium, and often encircles more or less completely the great vessels. The blood content of the organ is often found increased, and its surface or section may present the petechiæ characteristic of death by asphyxia. The histology of the enlarged gland indicates usually a simple hyperplasia of the lymphoid cells, enlarging and multiplying the follicles, sometimes causing the deposit of small nodules of lymphoid cells in the centres of lobules, in the trabeculæ, or even in the outlying adipose tissue.

The enlargement of the spleen is of moderate grade, and is referable to a simple hyperplasia of the lymphoid elements, with hyperæmia. The enlarged Malpighian bodies being usually devoid of blood and light colored, are prominently set off from the hyperæmic pulp, giving an appearance not unlike that of miliary tubercles. In some cases the lymphoid cells are so much increased as to infiltrate the splenic pulp, and the microscopical outlines of the follicle are then indistinct.

The pulp cells may contain an increased deposit of blood pigment, of which condition one of the present cases furnishes an extreme example.

The lymph nodes most frequently affected are the pharyngeal, thoracic, and abdominal chains. The faucial and

lingual tonsils are nearly always enlarged, the new cells not always being confined to normal limits, but sometimes forming a diffuse infiltration of the mucous membrane about the original follicles. From the lingual tonsil the infiltration may involve the epiglottis and sinus pyriformis.

The cervical, mediastinal, and axillary nodes may be moderately enlarged, especially along the course of the great vessels. Tuberculous lymphadenitis has been observed (Bayer).

The abdominal lymph nodes, especially those of the intestine and mesentery, are usually strikingly enlarged. In one of the present cases some of the Peyer's patches measure nine to eleven centimetres in length, and their follicles and the solitary follicles project very prominently above the surface of the mucosa. The swollen mesenteric nodes may remain entirely discrete, or, as in the present case, they may form a solid mass of lymphatic tissue, in which the separate nodes are closely applied one against the other, although the capsules remain intact. The enlargement is due to a simple hyperplasia; the lymph paths appear for the most part undisturbed, but the adjoining connective and adipose tissue may contain a moderate deposit of new lymphoid cells. The retroperitoneal nodes are often affected. The mesenteric nodes may be enlarged when the intestinal follicles appear normal. The nodes of the entire gastro-intestinal tract are frequently involved in the hyperplasia. The inguinal, popliteal, axillary, cervical, supraclavicular, and infraclavicular nodes may be moderately enlarged. Small collections of lymphoid cells have been found in the thyroid gland, which is frequently enlarged in these cases. Similar collections of lymphoid cells were noted in the capillaries of the liver in one of Kundrat's cases, aged fifteen years. In three of Kundrat's cases, aged fifteen, twenty-four, and thirty-one years, red marrow was found in the shaft of the femur. In only one of these cases, however, does it seem certain that this unusual condition represented a true lymphoid hyperplasia, as in Case

II, in which there was noticeable atrophy of fat cells and more or less diffuse lymphoid tissue in the marrow, containing neutrophile and eosinophile myelocytes and dense nodules of lymphoid cells. The marked variability of the character of the bone marrow in the femur has been amply demonstrated by the extensive studies of Grohé, and of Litten and Orth.

Relation to Pseudo-leucæmia.—Such a general and extensive hyperplasia of the lymphatic structures of the body at once suggests a possible connection with leucæmia or pseudo-leucæmia. The resemblance to these diseases is especially evident in those cases showing extensive enlargement of the mesenteric nodes or diffuse infiltration of mucous membranes with lymphoid cells, or collections of lymphoid cells in unusual situations, as in the hepatic capillaries and thyroid gland. The destruction of red blood-cells characterizing these diseases has been approached in cases of the lymphatic constitution, as indicated by the deposit of blood pigment in the spleen and lymph nodes, a condition well marked in the spleen in one of the writer's cases. Koeppe reports a similar case in which the deposits of pigment were very extensive, and also notes an increased number of leucocytes in sections of many vessels, without stating the character of the leucocytes, an observation to which it seems hardly possible to attach any significance. In one of the writer's cases eighty-four per cent. of a considerably increased number of leucocytes in a pial vein were small and mononuclear. Ortner observed in one case a lymphocytosis at a time when it was not known that a lymphocytosis is usually found in the blood during the second week of typhoid fever. In three of Kundrat's cases the extent of lymphatic hyperplasia might have sufficed for an early stage of leucæmia.

But even these many isolated points of resemblance constitute no distinct indication that the *constitutio lymphatica* has any immediate connection with pseudo-leucæmia or leucæmia.

Comparing the enlarged intestinal follicles in the writer's

first case with the intestinal lesions of some undoubted cases of pseudo-leucæmia, characteristic differences were noted. The small nodules of new lymphoid tissue in the latter disease grow laterally for some distance before producing much elevation of the mucosa, while in the former the enlarged follicles are very shortly circumscribed and very early project above the surface of the surrounding mucosa. The nodules in pseudo-leucæmia frequently ulcerate at their central points owing to deficient blood supply, a tendency entirely lacking in the enlarged but well vascularized follicles in the former condition. In most cases of pseudo-leucæmia of intestinal type there are some distinctly pedunculated polypoid outgrowths, considerably exceeding in size any of the hyperplastic nodules yet reported in cases of the lymphatic constitution.

In the majority of the cases of lymphatic constitution the enlargement of the lymph nodes does not pass beyond the limits of what may be called a physiological hypertrophy, and bears little resemblance to a tumor formation. The spleen is rarely much enlarged. The presence of considerable pigment in the spleen pulp is too ordinarily seen to be interpreted positively as the result of an excessive blood destruction, such as characterizes the severe anæmias. Yet it must be admitted that the very considerable degree of pigment deposit reached by the two cases referred to above indicates that in some instances the blood has suffered severely. These children are, however, not usually anæmic, but in excellent health, and even the sickliest of them do not resemble cases of infantile leucæmia, pseudo-leucæmia (von Jaksch), or chlorosis. As for the hyperplasia of the lymphoid marrow, it may be said that the normal limits of lymphoid marrow are as yet by no means definitely settled. Such hyperplasia may be seen also in the secondary anæmias, and in any case the hyperplasia of the lymphoid marrow may be regarded as merely a part of the general and more or less physiological hypertrophy of the lymphoid structures of the body.

It is worth noting, in this connection, the apparent possible explanation of some cases of lymphocytosis in children, which is so frequently observed at this age, and has at present little definite significance. It might be expected that a general lymphatic hyperplasia would lead to a lymphocytosis such as was present in the writer's case to a marked degree. That all children showing persistent lymphocytosis are subjects of the lymphatic constitution can not now be asserted. In the writer's experience, children with extreme lymphocytosis may at least survive severe attacks of diphtheria. Nevertheless, it must be regarded as possible that the persistent lymphocytosis of childhood may at times be a tangible expression of general lymphatic hyperplasia and of the lymphatic constitution.

Relation to Rhachitis.—In a considerable proportion of the reported cases of *constitutio lymphatica* more or less pronounced evidences of rhachitis have been found.

Professor Kundrat described as primary vegetative disorders those anomalies of growth whose cause we do not know, and which we must refer to a congenital predisposition. Rhachitis he specially emphasizes as representing not only a disturbance in bone formation, but a profound and general vegetative dyscrasia. This view of the pathology of rhachitis, which is, of course, the one in general acceptation, is here mentioned in order to emphasize the fact that the coincidence of rhachitis, which is not an essential feature of the lymphatic constitution, must be regarded, with the hypoplasia of the heart and arteries, as further evidence of some deep-seated constitutional weakness.

It is interesting in this connection to recall the fact without speculating upon its significance, that a large percentage of rhachitic children have a hypertrophic spleen, which is, however, according to the recent conclusions of Starck, not uniformly proportionate to the grade of rhachitis, but rather to the degree of anæmia.

The coincidence of rhachitis and enlargement of the spleen with hyperplasia of lymph nodes, especially the mesenteric nodes, was long since noted by Dickinson and Glisson.

Significance of Enlargement of the Thyroid in the Lymphatic Constitution.—In nine of the seventeen cases collected by Kundrat, in three of seven referred to by Paltauf, and in one of the writers two cases—*i. e.*, in more than fifty per cent. of twenty-six cases—the thyroid gland was found enlarged. Of the significance of the goître in this connection it is rather difficult to judge. There is, however, abundant evidence to show that some sympathetic relation exists between the thymus and thyroid.

Béclard found an enlargement of the thyroid after extirpation of the thymus, and enlargement of the thymus after extirpation of the thyroid, in animals capable of surviving the loss of these organs. As shown by Kundrat, enlargement of the thymus has been found in Basedow's disease by Möbius and by Spencer, and hypertrophy of lymph nodes, tonsils, and intestinal follicles has been noted in the same disease by several observers (White, Gowers). The liability to sudden cardiac paralysis, which is often the prominent feature in the death of subjects of the lymphatic constitution, finds at least a partial counterpart in the persistent tachycardia of Basedow's disease. Müller believes that a congenital or acquired neuropathic constitution is an essential element in the production of exophthalmic goître.

Exciting Causes and Manner of Death of Subjects of the Lymphatic Constitution.—The majority of cases thus far reported have died as the result of chloroform narcosis. One case reported by Heusler died after ether narcosis and the loss of considerable blood. Death may apparently occur at any stage of the narcosis, during the first few inhalations or even after apparent recovery from the effects of the anæsthetic.

Two patients survived a first administration of chloroform to perish some months later during a second or third operation.

The usual signs of danger may be observed; the patients may respond to treatment for a time, and a few feeble respiratory movements may be elicited for some moments,

or for a considerable period, or the cardiac and respiratory paralysis may be instant and complete. In all of these particulars these cases have presented no distinguishing peculiarities.

Seven reports by Nordmann and Paltauf refer to the sudden death of persons who fell into the water, and although immediately recovered were yet dead, or who died suddenly while bathing.

In none of these cases were the ordinary signs of death by drowning to be found, but the usual evidences of the *constitutio lymphatica* were present.

Other persons died suddenly during the excitement of card-playing, or fell dead on the street while engaged in ordinary exertions.

The sudden death of the young son of Professor Langerhans, of Berlin, immediately after the injection of a preventive dose of diphtheria antitoxin has called forth considerable discussion as to the probable cause of this sudden fatality, and has been variously explained by Langerhans, Eulenberg, and Pürkhauser. Paltauf suggests that this and other similar cases may find their true explanation in the presence of the *constitutio lymphatica.*

It seems probable, from the considerations relating especially to hypoplasia, of the heart and arteries, that some rapidly fatal forms of the infectious diseases, and some sudden fatalities during convalescence from these diseases, may be in part referable to the *constitutio lymphatica.*

It must be emphasized, however, that the data are as yet entirely too limited to indicate definitely the scope of the *constitutio lymphatica*, and until the observations have been very considerably extended it will be well to observe extreme caution before attributing miscellaneous cases of sudden death to the lymphatic constitution.

The manner of death usually indicates a cardiac paralysis, which may or may not be combined with immediate failure of respiration. Of the chain of events by which this result is reached little is known. That the cardiac muscle in these

subjects is specially susceptible to the effects of chloroform may naturally be supposed. Very slight importance can at present be attached to the mechanical irritation or pressure of the enlarged thymus. We are therefore compelled to content ourselves with the statement, very plainly supported by clinical experience with these cases, that the subjects of the lymphatic constitution, for unknown reasons, are specially susceptible to reflex cardiac paralysis.

The Diagnosis of the Lymphatic Constitution.—Since it is claimed that the majority of deaths from chloroform are referable to the *constitutio lymphatica*, it becomes a matter of importance to be able to recognize the condition during life. Unfortunately, in the present state of our knowledge this is in many cases impossible, yet a thorough examination of the patient will probably disclose one or more suspicious signs.

It may be possible, first, to elicit physical signs indicative of hypoplasia of the heart and aortic system of arteries, although the conclusions thus reached will be regarded by conservative clinicians as very uncertain.

Fraenkel, Rauchfuss, and Quincke call attention to the dilatation of the left ventricle, which usually results from a narrowing of the aorta. They also recommend the examination of the peripheral arteries, which may be found distinctly narrowed and of increased tension. Ortner has noted in his cases of narrow aorta, an absence of aortic pulsation in the neck, which he regards as a pathognomonic sign of hypoplasia of the aorta, if found in a muscular subject. As already mentioned, hypoplasia of the heart and arteries is frequently associated with an infantile or defective development of other organs and tissues, especially of the sexual organs, the condition of which it may therefore be well to ascertain.

In some of the reported cases the diagnosis was suggested by the absence of pubic hair, by the very late establishment of menstruation, and from a uniformly contracted condition of the pelvis. Yet even granting that attention to the above

minutiæ may occasionally give rise to a strong suspicion of hypoplasia of the aorta, it is not to be supposed that every case actually presenting this anomaly is a subject of the lymphatic constitution, so that, practically, the diagnosis of this anatomical feature will usually be restricted to the post-mortem table.

Likewise, the prevalence of rhachitis is too general to warrant more than a suspicion that this disease may be associated with the lymphatic constitution, and its presence can only serve as a warning that the two conditions sometimes coexist, rendering the subject a dangerous one for the administration of chloroform.

Of greater diagnostic import is the discovery of a general or local hyperplasia of the superficial lymphatic structures. Enlargement of the faucial, lingual, or pharyngeal tonsils, especially if accompanied by enlarged cervical, axillary, or inguinal lymph nodes, should at once arrest attention. In one of Kundrat's cases there were distinct flat deposits of lymphoid tissue along the base of the tongue and about the epiglottis, and in another the retropharyngeal nodes were moderately enlarged. In one of the writer's cases the enlarged mesenteric nodes formed a tumor-like mass that could readily have been detected by abdominal palpation. In young subjects it may sometimes be possible to elicit dulness from the enlarged thymus.

The demonstration of a well-marked lymphocytosis in one of the writer's cases, a condition which may reasonably be expected to frequently accompany general lymphatic hyperplasia, suggests that the examination of the blood may give a reliable indication in some cases of the *constitutio lymphatica*. The lymphocytosis of early life, which has been rather frequently observed, has as yet acquired little or no significance, and although the suggestion is based upon a single observation, that alone would seem sufficient to urge that the condition of the blood should be noted in every suspected case.

In conclusion, it must be admitted that while the studies

of the Vienna observers seem to have placed the existence of the *constitutio lymphatica* upon a firm basis in pathology, the observations yet remain far too limited to fully demonstrate the truth of an hypothesis which connects a large class of sudden deaths with simple hyperplasia of the lymphatic structures of the body.

It has been deemed advisable, therefore, to place the present cases on record, and it has been the further object of this paper in outlining the chief anatomical features of the lymphatic constitution to urge the claims of the subject to more general attention, especially from those in charge of medico-legal autopsies.

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Dr. POWER recalled an autopsy upon a case of Basedow's disease, in which the thymus gland was considerably enlarged. The subject was a woman, twenty-one years of age. The uterus and ovaries were undeveloped, and the kidneys were lobulated. No other enlarged glands were found. He did not think that, as yet, we were justified in placing either the thyroid or the thymus glands among the lymphatic glands.

Dr. EWING said he was not able to say just where the thymus and thyroid glands were to be classed. He thought a word ought to be said on the negative side of this subject. The lymphatic constitution did not seem to him as yet an

established fact. Many of these cases of sudden death under chloroform had been previously subjected to severe tests of vitality, and had not succumbed. Another fact in connection with these reports from Germany which was of some importance, was the freedom with which chloroform is administered in that country. The diagnosis of *constitutio lymphatica* was accepted without comment in Vienna at the present day, and hence the condition should receive more attention here.

FŒTAL ENDOCARDITIS.

Dr. MARTHA WOLLSTEIN presented a heart taken from a baby, six weeks old, who had been admitted to the Babies' Hospital. On admission there was a loud systolic cardiac murmur, heard with greatest intensity at a point just below the left nipple, but audible all over the chest. Cyanosis was present only just before death. The autopsy showed the heart to be enlarged; the left ventricle decidedly hypertrophied; the aortic orifice stenosed to about half its normal size, and the semilunar valves so agglutinated that there were only two flaps instead of three. All the other valves were normal.

THE DIPLOCOCCUS INTRACELLULARIS MENINGITIDIS.

Dr. WOLLSTEIN also presented a brain from a boy who had been admitted to the hospital when five months old, after an illness of seven weeks. According to the history, the child had been perfectly well up to the beginning of this last illness. The onset was sudden, and was marked by crying, vomiting, and the classical symptoms of meningitis. Three days before this, the child had fallen out of bed on to the floor. On admission, the child, although five months old, weighed only eight pounds eleven ounces. There was marked opisthotonos; the left patellar reflex was exaggerated; there was a spastic condition of all the muscles; the child was entirely blind; the pulse was 200 and irregular; there were no râles anywhere in the chest. The

temperature just before death reached 105.4° F. There had not been any true convulsions, although there had been twitchings. The day before his death there was a hemorrhagic discharge from one ear. The autopsy revealed a thin, purulent exudate over the entire surface of the brain, most marked on the convexity. While removing the brain an abscess was opened into on the inferior surface of the cerebellum. It was about the size of a hazel-nut. The pus was greenish and very viscid, and the convolutions were visibly flattened. Both lateral ventricles were filled with this same viscid pus. The third and fourth ventricles and their communication were also distended. Permission could not be obtained to remove the spinal cord, but the membranes, detached through the foramen magnum, were infiltrated. The lungs were not consolidated anywhere, but they were very hyperæmic, and somewhat œdematous. A small infarction was found in the upper border of the left lower lobe. The liver was fatty. There were no other lesions. The petrous portions of both temporal bones were examined and found to be normal. On making cover-glass smears from the pus, and staining by Baumgarten's method, very few organisms were found, and these were all diplococci. They did not resemble the pneumococcus. They were not decolorized by Gram's stain. Cultures on glycerine agar from the ventricles and cerebellar abscess showed in twenty-four hours a grayish growth, which was much more abundant than would have been obtained from a pneumococcus culture at this time. On the second day, there were larger colonies than would have been present from a pneumococcus culture. In neutral bouillon the growth was more luxuriant than a pneumococcus growth. A white mouse was given a subcutaneous injection of a pure bouillon culture. It remained well. After seven days it was killed, and the blood was found to be perfectly sterile. Dr. Wollstein concluded, therefore, that the organism in this case was the *diplococcus intracellularis meningitidis*, described in 1887 by Weichselbaum. This organism

was found by Jaeger to be longer lived than the pneumococcus, and where chains were formed there were longitudinal lines of division. Weichselbaum described the diplococcus as decolorized by Gram's stain, but Jaeger had stated that the smears remained stained, although the sections were decolorized. It was very difficult to demonstrate the organism in sections. Anilin oil and gentian violet, followed by acetic acid and alcohol, constituted the best stain for the sections.

A CHONDRO-EPITHELIOMA (?).

Dr. HENRY POWER presented a microscopical section of a tumor found in the subcutaneous tissue in front of the angle of the jaw in a girl of eighteen. The tumor had been there for some time, but had grown rapidly during the last two months. It was encapsulated, and had a distinct hilum. It was easily removed. On section, it was quite dense. There was a considerable quantity of cartilage in the tumor, both normal and degenerated, and scattered through this was a deposit resembling in some respects carcinoma. He presented the specimen for a diagnosis.

Dr. EWING said that he had seen a tumor from the supraclavicular region, which had presented an almost identical structure. The specimen presented suggested, of course, the possibility of its being an endothelioma.

The PRESIDENT also looked upon the specimen as probably an endothelioma.

GLOBULAR THROMBUS IN THE HEART.

Dr. HARLOW BROOKS presented a tumor removed from the right auricle of the heart of a boy. When eight years old, the child had had an attack of scarlatina. About two weeks ago there was found to be considerable œdema, and he was brought to hospital. Examination of the urine showed evidence of acute nephritis. Physical examination of the chest showed mitral stenosis and a double aortic lesion. It was found necessary to tap the abdomen twice,

and to drain the fluid from the lower extremeties. Bacteriological examination of the urine and of the fluid taken from the abdomen was negative. At the autopsy, the remarkable feature was the heart, which was very much dilated on the right side, while the left side was contracted and the aortic segments were much thickened. The mitral valves were very indistinct, and the papillary muscle had also become fused by an endocarditis. The right auricle contained the specimen presented—a mass which appeared to be a globular thrombus. It lay in the auricle perfectly free. In the fresh state its surface had presented a slightly papular appearance.

A hasty reference to the literature seemed to indicate that this was a very rare condition. He found it difficult to understand how such a body could exist in the auricle during life without having been detected by physical examination. There were many areas of hemorrhagic infarctions in the lungs.

The PRESIDENT said that he had never seen just such a thrombus, although he recalled having seen a pedunculated thrombus presented to this Society some years ago. The explanation of these cases, as offered by Dr. Osler, was that there was originally a thrombus with a slender pedicle, and that this had been broken off.

The Society then went into executive session.

Stated Meeting, December 23, 1896.

JOHN SLADE ELY, M.D., PRESIDENT.

A PANCREATIC CYST.

Dr. WARREN COLEMAN presented a pancreatic cyst removed from a woman sixty years of age, who died of pulmonary tuberculosis in Bellevue Hospital, in the service of Dr. W. Gilman Thompson, through whose kindness he was permitted to report the case. Aside from the condition of the pancreas, the details of the autopsy were uninteresting in this connection. While removing the intestine a distinct prominence was noted in the pancreatic region between the stomach and transverse colon. It was found to be a cyst with fluid contents. The cyst, with the adjacent structures, including a portion of the duodenum, was removed. It was bilocular, consisting of a large and a smaller division, communicating by a large opening. A dense band of fibrous tissue extended across this opening. The cyst contained, but was not entirely filled by, a yellowish-brown, turbid liquid, in which were numerous small, shining, flattish yellow crystals. The wall of the cyst consisted of dense fibrous tissue, with circumscribed thickenings on its inner surface. The total length of the cyst was 11.5 ctm., the larger division measuring 8 x 10, and the smaller 3 x 6 ctm. The thickness of the wall was 2.5 ctm. On the inner side of the wall of the cyst, toward the duodenum, was a distinct papilla with a central opening, which admitted a filiform bougie. The bougie passed out into the duodenum, through the biliary papilla. The ductus communis choledochus joined the pancreatic duct in the wall of the duodenum. At first it appeared that all of the pancreatic tissue had disappeared, but on careful dissection it was found that several small masses were still present between the cyst and duodenum, and that there was a small single mass at the extreme tip of the smaller division of the cyst. Sections taken from the wall of the larger and smaller divisions of the cyst show that

there was no definite lining membrane. The wall was composed of dense fibrous tissue, which toward the cavity of the cyst, however, formed a more or less open meshwork, in which were chiefly small round cells and a few larger round, flattened cells. Young connective-tissue cells were also to be seen.

From these appearances it would seem that the cyst wall was adding to its thickness from within. The circumscribed thickenings on the inner surface of the larger division possessed essentially the same structure. They contained, however, numerous pigmented cells and a few giant cells, and were plentifully supplied with blood. The pigment, when tested with potassium ferrocyanide and dilute hydrochloric acid, failed to give the reaction for iron.

Albumin and mucus were present in abundance in the cyst contents. No sugar was found by Fehling's test, nor did Gmelin's test reveal the presence of any bile-pigments. The crystals already mentioned were cholesterin. In addition, numerous small acicular crystals were present. A small number of round, flattened epithelioid cells were found. A moderate number of white and red blood-cells were found, but they were supposed to have gained entrance on the knife and scissors used to open the cyst.

Experiments were undertaken to determine the physiological properties of the liquid. Three test-tubes were filled with a dilute solution of boiled starch, and varying amounts of the cyst contents were added to them. They were put into an incubator for twenty-four hours, after which they were examined. The tube containing the greatest amount of cyst contents showed complete conversion of the starch into sugar, while the other two contained, in addition to sugar, some unaltered starch and erythro-dextrine. The tests used were Fehling's solution and iodine. Unfortunately, lack of time prevented examination for the presence of trypsin. The emulsifying ferment was not present. Fitz states, however (*American Text-Book of Medicine*), that in cysts of long standing one or more of the ferments might

be absent; and on the contrary, Boas and Jaksch believe that liquids possessing these physiological properties were not necessarily derived from the pancreas, since other pathological liquid accumulations might possess one or all of them.

Fitz also divides cysts of the pancreas into three classes, viz.: the retention cyst, the cystoma resembling cystomata of the ovary, and a form which appears to be on the border line between these two. Both of the former varieties might be multilocular. This author says that, "in typical cases from dilatation the duct (of Wirsung) may be traced from the duodenum into the cavity of the cyst, and from the tail into the same cavity. At times the duodenal end of the duct is obliterated in the immediate vicinity of the cyst-wall."

The speaker said that it was somewhat difficult to assign the cyst under consideration definitely to any one of the three classes. No evidence had been left of any cause of retention, and moreover in sections from the remaining portions of the pancreas there was no retention—dilatation of the ducts. Neither could the cyst be classed with the cystomata, because of the absence of a lining membrane. It was probable, therefore, that the cyst did not belong to any of the above varieties.

Referring to the etiology, he said that the cyst was evidently of long duration from the thickness and density of its wall. In the absence of definite evidence, the question of the origin of the cyst must be a matter of conjecture. The most probable theory was that the cyst was of traumatic origin, though cysts arising in this region from traumatism were not, strictly speaking, pancreatic (Fitz), as a rule. The fact, however, that the remains of the pancreas were so widely separated, portions being at either end of the cyst, and the fact that the cyst cavity communicated with the duodenum through the usual channel, would seem to show that originally the pancreas was of normal size and position. The retention theory was not tenable because of the absence of a

calculus or a constriction in the duct between the cyst and duodenum.

The case was interesting also from another standpoint. The urine did not contain sugar, thus furnishing clinical confirmation of the fact established experimentally by von Mering, Minkowski, Hédon, and others, that if a small portion of the pancreas remain, whether in its normal relations, or grafted under the skin, glycosuria did not occur. And this confirmation was all the more remarkable from the fact that sections from the remaining pancreatic tissue showed extensive degeneration. It was unfortunate that such symptoms of pancreatic disease as probably had been present could not have been noted. But the woman had been in the hospital only a day or two, and the pulmonary affection demanded the chief attention.

The PRESIDENT said that a short time ago he had examined the contents of one of these cysts chemically, and had found neither the amylolitic or the proteolytic ferment present, and he had not detected any change in the starch after standing overnight. He believed that the presence of the ferment was not at all constant in the contents of such cysts. It had just occurred to him that the cyst under consideration might possibly have been the result of a necrosis of the pancreas—as a secondary degeneration. He did not see why a cyst should not form in this way, as well in the other ways already referred to. Such a change was occasionally seen in infarctions. Another possibility was an abscess formation.

Dr. COLEMAN replied that the objection to this theory was that there was an increase in the size of the cyst without any obstruction to the outflow of the contents. He had thought first that it might be of congenital origin, but had abandoned this idea because of the wide division between the parts, making it seem that the pancreas had originally been of normal size.

The Society then adjourned.

MIDDLETON-GOLDSMITH LECTURES: ON THE RELATIONSHIP BETWEEN INFLAMMATION AND SUNDRY FORMS OF FIBROSIS.

By J. GEORGE ADAMI, M.A., M.D., Camb.,

Professor of Pathology, McGill University, Montreal.

LECTURE I.

Mr. President and Gentlemen: I cannot proceed to the delivery of these lectures without in the first place extolling the beneficence of him through whose regard for this Society and generosity it has been made possible for you to institute this series of lectures—of him whom thus you are bound to keep in ever green remembrance. And in the second place I owe it not only to you but to myself to give utterance to my very sincere gratitude for the honor done me in inviting me to attempt to fill a position in which already the great pathologists of this continent have one after the other added new leaves to their laurels. For myself I cannot hope to vie with my illustrious predecessors. I can but exceed them in appreciation of the honor done to me, and through me to the city and university of my adoption. I feel acutely your kindness in thus inviting to deliver these lectures one who is a stranger among you, one who as yet can scarce feel himself other than a stranger to this continent. For my university it does not need that I should be specially empowered to announce to you how, striving toward higher things, that university appreciates and is encouraged by every act of recognition from the larger world.

It might, perhaps, sir, be expected, by that larger world that I should here make due and telling reference to my presence among you at the present epoch. I am inclined to

think that when the universality of science and our common brotherhood in it are so obvious to all of us, and the insistence thereupon is to us so much of a truism, it were almost an insult to your intelligence and good will did I say anything, however much I may personally appreciate your kind invitation at this especial juncture. The most I dare venture is to express the fervent wish that the same fellowship may bind together the nations which now unites all those striving after good works in all branches of science.

Throughout the days of this generation, and to an increasing extent in these latter days, there has been and there continues to be a lively discussion as to what is and what is not to be included in the scope of inflammation. And as of late among a narrow sect of surgeons or surgical pathologists there has been manifest the revival of what, were I a theologian, I should denominate a (not unqualified) heresy, but what, as a pathologist, I prefer to describe as, in my opinion, a serious misconception, I have thought it well, not only from the interest excited by the subject in our body, but also from the recrudescence of this misconception, to select as the subject of these lectures, this matter of inflammation and the relationship existing between it and fibrosis or fibrous hyperplasia in its various forms.

Even at the best this is a subject involved in difficulties. How involved I did not wholly realize until some months ago I was called upon by my friend, Prof. Clifford Allbutt, of Cambridge, England, to discuss the matter succinctly in the course of an article upon the "Pathology of Inflammation in General," and was forced to face the matter straightly. As I doubt not, most here present have found it is one thing to have general opinions, another to place them in logical sequence upon paper. When I came to attempt the latter, and again to consult the accounts given in the leading articles and text-books, I discovered not only the inconsequential nature of many of my previous views, but also that most of what had already been written read like the writing

of scribes rather than those having authority : and after having written the article or section of an article already referred to I cannot but feel that what is there stated merits the same reproach, and since the manuscript left my hands the more I have deliberated the more dissatisfied have I felt over my own writing. I am glad to have this opportunity to revise and advance my views upon the subject, and even before the article in question is published to amend it and carry to a more logical conclusion the treatment of the principles upon which the article is based. I cannot hope to solve all or any of the problems that a study of this relationship between inflammation and fibrous-tissue growth opens up ; at most, suggesting rather than dictating, I may possibly help others toward solution and may indicate the lines along which future research would seem to promise satisfactory results.

We are accustomed to employ the termination "itis" with the prefix "chronic" in almost if not quite every case in which there is replacement of the cell elements proper of a tissue by new fibrous-tissue growth. That is to say, we assume all these conditions to be of like origin, to be manifestations of chronic inflammation, or as the attempt at repair following upon acute inflammation.

Fibroid areas in the heart muscle are all grouped together under the convenient term of chronic interstitial myocarditis. Fibrosis of the valves of the heart with its sequelæ we speak of as chronic endocarditis. Arterio-sclerosis is indifferently spoken of as chronic arteritis or endarteritis. Whatever the form of fibroid change occurring in the kidney, it comes under the heading of chronic interstitial nephritis. In the case of the liver it is true the conveniently noncommittal name of cirrhosis is in English-speaking countries the term most usually employed to denote fibroid change, yet there are not wanting those who speak of chronic interstitial hepatitis.

I might similarly pass in order organ after organ of the body, with its chronic "itis." Lax indeed is the employ-

ment of this common denomination of chronic inflammation, and its sole merit is its convenience in cloaking our ignorance of the exact causation of most of the conditions to which it is applied. In these lectures I wish to discuss how far and in what cases we are justified in the employment of the term, and to what extent the development of fibrous tissue in the more noble organs of the body is the result of inflammatory disturbance.

In such a discussion everything depends upon the definition of inflammation which is found acceptable, and the conclusions reached must stand or fall in the exact ratio in which the definition enunciated commends itself to other workers. Thus, first, it will be absolutely necessary for me to state clearly and distinctly what I understand by the term "inflammation."

Two courses, it seems to me, and only two are open to us with regard to our appreciation of the term. Either we can, with Thoma, agree that it is so unsatisfactory and that the discussions which have arisen as to its scope, or, more truly, as to the processes that are rightly to be included under the term, are so barren and profitless that we decide absolutely to expunge it from our vocabulary; or, on the other hand, we must determine to include in our idea of inflammation all processes having a like origin and tendency. There is no logical intermediate course unless it be to confine the term strictly to its primitive meaning and to determine that there can be inflammation only where there is "flaming," where there is redness and heat. No one is prepared nowaday to take this course, for this necessitates physiological active congestion of a superficial organ being considered as inflammatory. Nor again are there many who, wedded to tradition and cardinally virtuous, with Celsus only see inflammation when rubor, calor, dolor, and tumor are present. For these cannot deny that identical processes may occur when one or two or more of these cardinal symptoms are wanting. Thus, nowadays, those who would define inflammation etymologically are non-existent, while the partisans

of tradition are "minished and brought low," forming a small and an impossible remnant. Hence, to return to my previous statement, there are but two logical courses open to us. Can we accept the first alternative and banish the idea of inflammation? I trow not—the suggestion is too quixotic. It is not within the power of any workers in any one branch of our science, even if that branch be pathology, to expunge at will a term of universal employment, a term that has come down to us through the ages—a term which, however loosely and variously employed, does nevertheless for all cover a greater or less number of processes of common occurrence. We cannot in a widespread science suddenly create a "tabula rasa" and start anew. Just as were we to do away with the plutocracy and start equally endowed with worldly possessions, while in twenty years the old plutocratic families would perchance be non-existent as such, yet the amassing of money and possessions in the hands of a few would inevitably be manifested, so were we to banish "inflammation" from our vocabulary, in the same time or even less some other word would be surely in common employment to denote the same idea. It cannot be done, and as a consequence the adoption of the second alternative is our only practical course.

We have, that is to say, so to employ the term that it will embrace all processes having a like origin and like import. Thus, then, starting from the generally accepted basis that the process is in its essence local and that the prime cause of all inflammations is injury to the tissues, if we are prepared to admit that one common or allied train of results follows upon all injuries, we must as our provisional definition state that inflammation is the series of changes constituting the local reaction to injury.

This is to all intents and purposes Burdon-Sanderson's definition and is that which for the last quarter of a century has been most generally accepted. For myself I cordially accept it as a good working definition; but at the same time I cannot but consider that the researches made since 1880

have materially added to our comprehension of the phenomena associated with the process and of their tendency, and permit us now to acknowledge the import as well as the origin of the process. Those researches have shown us that a very definite meaning is to be attached to the main vital processes which follow injury to a part. They have proved that the accumulation of leucocytes in the injured area is purposeful; that, whether by intra- or extra-cellular action, these cells are capable, up to a certain extent, of counteracting the irritant and of removing dead and effete material; they have satisfactorily proved that the inflammatory serum possesses both digestive and bactericidal powers greater than the serum of the circulating blood: they have demonstrated that the migration of the leucocytes into the inflammatory area is not a passive process, but an active one directly dependent upon the extent of the stimulus exerted upon these cells by chemical alterations in their environment; they have demonstrated that the amount of fluid exuded into any one region of the body varies *inter alia* directly according to the intensity of the irritant—the more intense the irritant the greater the extent to which it is diluted; while, further, the part played by the fixed cells in the immediate neighborhood is equally evident and equally purposeful, tending manifestly to result in the cutting off of the damaged area from the surrounding healthy tissue and again to replace the tissue that has undergone destruction. Hence I am impelled to define inflammation as the local attempt at repair of injury, or, more fully, inasmuch as there is a certain small class of cases in which all the symptoms of inflammation are present as a consequence of nervous disturbance wholly unassociated with previous local injury,[1] as *the series of changes which*

[1] The most striking example of this class is to be seen in the experiment which has been frequently repeated, among others by my colleague, Dr. James Stewart, of assuring a susceptible individual under hypnotic influence that the hand or other region has been burned or blistered, when within a very short period the part becomes reddened, swollen, and, it may be, the seat of marked serous effusion.

constitute the local attempt at repair of actual or referred injury to a part. So that needless objections be not raised, let me emphasize the fact that I do not regard inflammation as synonymous with repair. Attempt at repair and repair are two very different things, and no more to be confounded than attempted suicide and suicide, or, not to approach too closely to a very delicate subject, than the Emperor William's recent telegram to the Boers and actual war between two considerable European nations.

This, then, is the definition I am inclined to lay down. Save in the small matter of the wording, I do not claim any originality, for others in different lands have given forth definitions embracing the same idea. Thus Neumann, in Germany, defines inflammation as "the series of local phenomena which are developed in consequence of primary lesions of the tissues and which tend to heal these lesions."[1] Bland Sutton, in England, is somewhat more restricted. "It is," says he, "the method by which an organism attempts to render inert noxious elements introduced from without or arising within it."[2] I doubt whether Sutton is right in speaking of it as a method and to me the larger view appeals, not simply of counteraction against the irritant but also of attempt to bring about a return of the region toward a functional condition—but the definition contains the same recognition of the purposive nature of the process. And lastly, here at home, Councilman acknowledges the same. In his most lucid article in Dennis's *System of Surgery* he defines inflammation as "the sum of the phenomena which take place in the tissue as the effect of an injury. The object of these various phenomena is to overcome or to diminish the effects of the injury."[3]

Whatever justice there might have been a few years ago in the objection that this view of inflammation is teleological, now, with the facts at our disposal, the objection is no

[1] Ziegler's *Beitrage*, v., 1889, p. 347.

[2] I here quote from Professor Senn, not having been able to discover the original passage.

[3] Dennis's *System*, vol. i., 1895, p. 144.

longer valid. As well may the statement that the function of the heart is to propel the blood into the arteries be condemned as teleological, or objection be taken to the statement that digestion is the series of processes whereby matters received into the alimentary tract tend to be converted to the uses of the tissues of the body. We are ready enough to admit the deductions drawn from physiological experiments; we must equally accept the results of experimental pathology.

But the definition here enunciated is altogether too broad for many to accept, and ever since Hüter propounded the view that the term inflammation ought to be restricted to those conditions in which there is infection by microorganisms, with pus formation, there have not been wanting adherents of the narrower view. And as what is to follow must largely stand or fall according to the acceptance of the definition herein set forth, and inasmuch as this confounding of infection and pyogenesis with inflammation appears to be growing more and more popular upon this continent, I needs must for a short time discuss the propriety and soundness of the movement.

I do this, sir, with some hesitation, for I feel that I am reverting to very elementary pathology: nevertheless it is just because the matter is so elementary, so fundamental, so all-important for a right comprehension of all pathology, and because the distinction with which you have honored me affords an almost unique opportunity for calling attention to this matter, that I make bold to utilize this opportunity to urge a broad and logical consideration of the subject. Dr. Senn, professor of the principles of surgery in the Rush Medical College, Chicago, whose writings have obtained a wide circulation and whose influence in the North and West perhaps transcends that of any other surgeon, states in his *Principles of Surgery* that inflammation, in the widest and most comprehensive meaning of the word, should be made to embrace pathological conditions which are caused by the action of pathogenic microbes or their ptomaines upon the

histological elements of the blood and fixed-tissue cells, and that "true inflammation is always caused by the presence of one or more kinds of pathogenic microbes," a statement which, it may be added in parenthesis, does not prevent him from employing figures from Hamilton and others to illustrate the stages of the process, although those figures represent the results obtained by the use of chemical and not bacterial irritants.

Dr. Roswell Park, professor of surgery in the University of Buffalo, in a straightforward address read before the American Surgical Association in May of last year [1] is inclined toward the same opinion, and, as he at the onset especially invites kindly criticism, I may say that his challenge has perhaps more than anything else led me to take up the subject here. He urges first the revolutionary thesis that the combination of the four cardinal symptoms should not be regarded as indicating inflammation. We should dismiss from our minds the associated idea, and should refer to the redness and heat as hyperæmia, the swelling as exudation, the pain as the result of pressure. Only when these become developed or modified by the growth of micro-organisms in an injured area or by the action of their products should we venture to speak of inflammation. And the term should then comprise not only the local but also the general effects produced by the growth of the micro-organism. In fact, the existence of these general effects (as, for example, the rise of bodily temperature associated with the appearance of a small furuncle upon the nose) is given as a distinction between what Dr. Park regards as true inflammation and the non-inflammatory reactions of the tissues to non-microbic lesions.

While epitomizing Dr. Roswell Park's argument, I believe that I have accurately stated his main contentions.

Let us see what is the logical outcome of this idea. First and foremost the frequent association of redness, swelling, heat, and pain which may result from microbic invasions of the body is not in itself to be regarded as symptomatic of

[1] *Medical Record*, New York, i., 1895, p. 705.

inflammation. The association is common to microbic and many other lesions. Only the extension of this series of symptoms in special directions under the continued influence of bacterial irritation is to be considered as inflammatory; or, to carry this view to its logical conclusion, the surgeon must no longer depend upon the presence of cardinal symptoms; he must only call a region inflamed when he has either personally or through a bacteriologist determined the existence of bacteria therein. There is no attempt made by Dr. Roswell Park to limit inflammation to pyogenesis, and while this view of inflammation for surgical purposes, in the main, undoubtedly separates suppurative from other lesions, it is in the terms of this definition impossible to regard suppuration in itself as an inflammatory manifestation simply because, as is well known, suppuration may be induced by caustics and severe chemical and physical irritants, apart from the action of bacteria. As above stated, the bacteriological is to become the sole sufficient test of inflammation. While it is true that the general adoption of this view would result in rendering it absolutely necessary that every general practitioner should continually practise himself in elementary bacteriology, or else should banish the term inflammation from his diagnostic vocabulary—a not undesirable consummation, it may be,—I cannot but fear that the general practitioner will still continue to speak of the inflammation of scalded surfaces, of black eyes, and of fractured limbs; for he will still require some useful and generally accepted term to embrace the train of symptoms following upon every-day injuries. This attempt on the part of members of one branch of our profession to delimit our idea of inflammation largely for practical purposes must fail when put into practice.

Or let us examine the proposal from another side. "Without infection," says Dr. Roswell Park, "no genuine inflammation; with infection, inflammation and, what always goes with conflagration, more or less destruction. Congestion and exudation provoke little, ordinarily no constitutional symptoms; inflammation always does. . . .

I would," he states later (after discussing hyperæmia, congestion, and "cirrhotic" changes), "in an entirely distinct chapter and in an unmistakably separate way, take up the matter of inflammation—*i.e.*, infection." To all intents and purposes Dr. Roswell Park would substitute a word which, I think most will agree, has wisely been restricted to local disturbances for a word which has shown itself most useful as indicating the changes which may occur in the organism at large in consequence of microbic invasion. Up to the present time inflammation has been understood to indicate the local changes following upon an injury; fever and infection to indicate the more remote effects upon the organism at large. And I am forced to point out to Dr. Roswell Park that in "infection" he has a most useful word which will indicate everything that he wishes to include in his restricted idea of inflammation, and, that being so, there can be no valid reason why he should, with those "big, merciless hands" attributed by the late poet laureate to one of our surgical brethren, appropriate a word to which can be given a wider and at the same time a more exact use. The terms "wound infection," "local infection" and "general infection," and "infective inflammation," are in common and satisfactory employment and there can be little or no doubt as to their meaning. I beg Dr. Park to consider this before urging further the adoption of his proposals.

But while one is only too glad to have a word "infection" capable of covering the series of local and general effects induced by the presence and growth of micro-organisms within the body, its employment in nowise tells upon the fact that every change in the blood elements and tissues brought about by microbes and their products may be induced by irritants of another nature. While it is true that micro-organisms frequently lead to pus production and that suppurative inflammation is almost entirely induced by these agents, it is equally true, as was first clearly proved by Councilman, that sundry chemical substances can occasion-

ally set up an identical process. And as Leber has shown, the purulent fluid produced by this latter means has definite powers of breaking up and digesting proteid matter ; no clear distinction can be made between the septic and the aseptic pus save that the one is of microbic origin, the other not. A broad idea of inflammation to include all like processes throughout the higher animals must take cognizance of these facts.

Nor again, may I add, is it possible to distinguish one series of micro-organisms as essentially pyogenic. To attempt this is to draw a line between human and comparative pathology. While it is true that certain forms in man are peculiarly liable to induce abscess formation, those same forms by no means necessarily exhibit the same liability in other animals, and even in man they do not always lead to pus formation ; in short, suppuration is the expression, not of the presence of certain specific microbes, but of a definite grade of intensity of irritation, or, in other words, it is a phenomenon representing a certain ratio between the virulence of the irritant and the resisting powers of the organism. Increase the virulence of a micro-organism or diminish the resisting power of the organism, and in members of the same species similarly treated we may have every grade of acute inflammation, from local hyperæmia and slight diapedesis of leucocytes through local abscess formation, to spreading sero-purulent cellulitis and general septicæmic infection. Much has been done experimentally to prove the truth of this statement, while the recent work in the laboratories of this continent upon cases of typhoid and gonorrhœa has abundantly shown how micro-organisms which in ordinary are not pyogenic can be the prime causes of abscess formation. Indeed it may be said with some truth that the main bacteriological work of the past year has been in the direction of confirming this statement and in demonstrating in case after case this liability on the part of bacteria ordinarily non-pyogenic to lead to abscess formation.

If this be so and if bacteria can thus be the cause of a series of reactive changes on the part of the tissues, advancing by imperceptible gradations from the simplest transient local inflammatory change up to the most profound generalized septicæmic disturbance, and if again, as all must admit, they can induce either profound local destruction of tissues or well-marked local tissue overgrowth, then surely it is impossible to separate the lesions produced by micro-organisms from the parallel and identical series capable of being produced by other noxæ.

I trust, therefore, that I have made it clear that we are compelled to range together the series of changes induced locally in the tissues as the result of injury under the common heading of inflammation, and this irrespective of the nature of the irritant.

For pathologists in general, for those studying not merely gross anatomical lesions but finer also, for those dealing with lesions of internal organs as well as with lesions having an outward manifestation, for those whose pathology and study of medicine are not confined to man and who strive to base their knowledge of disease and its processes upon a study of the same throughout the animal kingdom, no other course is open and practical.

Following this train of thought it becomes evident that we must regard as of inflammatory origin all those changes in the tissues which we can prove to result from direct injury to those tissues, whatever the nature of the irritant, and which we can regard as tending toward repair. We can separate the various degenerations of the tissues, for these form a well-defined series of changes from the inflammatory lesions proper; we may regard them as associated with, but not inherent in, the inflammatory change.

Of these local attempts at repair the most durable and, when the process has come to an end or when, being of moderate intensity, it has continued for some little period, the most evident is the formation of fibrous tissue. Now, in studying this formation and the broader subject of fibro-

sis [1] in general, the first point to be settled, one which will materially affect our whole comprehension and classification of the fibroses, is whether it is possible to distinguish between new connective-tissue formation which is directly the result of injury and that which is indirectly the result, and if we can determine this we can with greater freedom attack the question of the classification of the fibroses in general and can more surely state which of them are to be considered of inflammatory origin and constituting chronic "-itides," which non-inflammatory.

The first question is one of peculiar difficulty, and the problem presented for solution may perhaps be best approached by a consideration of two widely separated cases. A study of the various stages of the development of a tubercle demonstrates that in man and most mammals the first result of the lodgment and growth of the tubercle bacilli in the tissues is to stimulate tissue formation. Only at a later period, with continued action of the products of the germs and associated disturbed nutrition of the central area of the granuloma, does tissue destruction become manifest. There is perhaps no better demonstration than this, unless it be that afforded by lepra nodules, of injury leading directly to connective-tissue growth.

On the other hand, we may consider the processes which occur in the central nervous system following upon atrophy and destruction of ganglion cells or upon separation of axis-cylinder processes from their trophic nerve cells. The results can best be seen when the injury affects secondarily all the members of an ascending or descending tract, and they are to be summed up as consisting of degeneration of the fibres forming the tract with replacement of fibrous tissue.

[1] Here let me state that I have no liking for this mongrel term "fibrosis"; nevertheless, I know of none which can satisfactorily replace it. The terms "sclerosis" and "cirrhosis" indicate only the secondary consequences of fibroid overgrowth, and "fibrous hyperplasia" is a little clumsy, while "fibrosis" undoubtedly conveys clearly its meaning; and in its favor (although two blacks do not make one white) it may be urged that in common usage we have such other mongrel terms as "fibroma," "fibro-enchondroma," and so on.

Here there has been no irritant circulating in the lymph bathing the fibres and leading directly by its action to their destruction. The degeneration and atrophy has followed upon injury inflicted at a distance, an injury to another region of the body. If any irritant be present it is of intrinsic origin. All the same, we see that the atrophied fibres become replaced by connective tissue.

Are we to regard this "replacement" fibrosis as a form of chronic imflammation? Against so regarding it it can be argued that, as already stated, no specific irritant of external origin can be adduced as having acted upon the tract of degeneration, and that in case after case where the degeneration has been gradual none of the ordinary symptoms of inflammation are recognizable, neither the coarser conditions of hyperæmia and exudation nor those finer ones of determination of leucocytes (though this phenomenon is at times quite distinct), multiplication of capillaries and other microscopical evidences of removal of destroyed tissue, and active new growth. Almost imperceptibly the atrophied nerve fibres are replaced by connective tissue, and it may be that of all the accompaniments of ordinary inflammation the sole distinguishable is the "functio læsa."

But there is another aspect of the condition that we are forced to regard, and I may best approach this indirectly. What satisfactory distinction, it may with justice be asked, can be drawn between this more insidious replacement fibrosis and the grosser replacement occurring in the case of infarcts? In the latter the normal course of events is, that, infective agents being absent, the necrosed area becomes surrounded by a zone of hyperæmia, the dead tissue undergoes disintegration and absorption and is replaced by new fibrous tissue. In such a case, it is true, we can recognize the distended peripheral vessels, the invasion by leucocytes, the formation of new vessels, all the main microscopical and most of the macroscopical signs of inflammation. But, as in our previous example, no extrinsic agent has set up the disturbances. It is difficult, indeed impossible, to arrive at any

other conclusion than that the products of necrosis act as the irritant and that they must be regarded as the cause of the inflammation and subsequent fibrous-tissue development. It is competent for us to assume the existence of a cryptic inflammation in the former case, and to hold that a like cause, namely, tissue necrosis, has led to a like effect, namely, fibrosis. And indeed if we adhere to the definition of inflammation that I have laid down, both of these cases of replacement fibrosis so obviously represent the local attempts at repair following upon injury to the tissues, that unless we further define what is meant by injury we are forced to regard them as equally of inflammatory origin.

We see thus that two different types of fibrous-tissue development, one hyperplastic, the other, as I have termed it, replacement, may be of inflammatory origin, and the more one examines into the subject the more difficult is it found to recognize inflammatory fibroses by their histological characters. While it is true that in certain cases we have histological evidence of progressive inflammation—the presence of newly formed vessels, of an increased number of extravascular leucocytes and small round cells, and it may be of a certain amount of exudation,—in cases of the same nature at a later date all these signs may be wanting, and again, in other allied cases, from the very onset both microscopical and macroscopical indications of inflammation may be peculiarly rare. We cannot depend upon histological evidence alone. At the most we can classify the various forms according to the evidence in our possession as to their origin and tendencies.

The considerations I have brought forward up to this point would lead us to distinguish at least two main types of fibroid change associated with inflammation, one of which, in default of a better name, may be termed productive, the other replacement, fibrosis. In the former there is no causal relationship between the amount of new connective-tissue resulting from the inflammatory action and the amount of tissue displaced; in the latter the amount of new

fibrous tissue developed appears to be primarily governed by and proportioned to the extent of the destructive process, but both equally tend toward repair and arrest of injury.

This division will, I think, be found useful, and it will be seen that the leading forms of inflammatory fibroid change are to be grouped under one or other of these heads.

Under the first are to be included sundry localized fibroses of which the main forms are the focal areas of new connective-tissue growth induced by the presence of certain microorganisms, that is to say, the more chronic or less acute forms of infective granulomata—the new growths (tubercles) induced by the tubercle bacilli, those (gummata) induced by the not surely determined organism of syphilis, the fibroid nodules caused by the presence of the leprosy bacilli, and, again, the more chronic type of actinomycotic and glanders lesions. Examples are not wanting of similar focal areas of fibroid growth induced by simple irritation. As such may, I think, be safely cited the earliest stage of one form of cheloid. Although, as I shall point out later, cheloid growths must be included among the fibromata; nevertheless, in many cases of what is sometimes termed and regarded as spontaneous cheloid, localized connective-tissue growths can be excited by local irritation of the surface. This was well observed in a case which has recently been very fully studied by one of my students, Mr. R. H. Martin. In this, the mere scratching with a pin was sufficient to give rise to the new growth. I am myself fully prepared to regard sundry cases of focal growth as non-inflammatory—as due to stimulation rather than to injury. The difficulty is that there is no line separating the one from the other; there is no sharply defined boundary between simple hyperplasia and that which is obviously reparative.

Merging at times imperceptibly into the previous group there are the capsular fibroses, comprising those cases of connective-tissue development induced around an irritant,

whether infective or not. Here the zone or capsule of tissue formation is a development of so much new material, laid down, it would seem, irrespective of previous tissue destruction in the immediate region of its appearance. Examples of this form will be immediately called to mind. Among the infective we have the thick capsules forming around obsolescent tuberculous masses, around chronic abscesses and phthisical cavities; among the simple irritative are to be classed the capsules developed around such foreign bodies as exercise little more than a mechanical irritation, whether those bodies be solitary and of large size, as, for example, impacted bullets, or minute and very numerous, as inhaled particles of coaly or silicious matter. Whether the capsules formed around and merging into the framework of benign tumors are to be classed as of simple irritative or of infective origin may possibly give rise to debate; provisionally I must refer them to the former class.

Another type of productive fibrosis, one that cannot satisfactorily be classed either as localized or generalized, is that due to inflammation of serous surfaces, a form including the fibroid thickening of serous superficies and organized inflammatory adhesions.

Besides these, there exist also generalized productive fibroses of inflammatory origin, which again may either be of infective origin (induced by bacteria or their products) or the result of continued non-infective irritation. The chronic interstitial pneumonia following upon subacute pleurisy may be cited among the former; among the latter, in all probability, the generalized interstitial fibrosis of so-called chronic parenchymatous disease, of which a good example is afforded by the condition of productive parenchymatous nephritis. But, as I shall have later occasion to point out, some forms at least of interstitial fibrous overgrowth are rather to be counted among the replacement than among the productive forms.

The local and general forms may merge, the one into the other. Thus, a liver presenting gummata may exhibit also

well-marked generalized interstitial fibroid overgrowth; a kidney the seat of chronic tuberculosis may show the same; or again, in the inhalation pneumonias the deposit of foreign particles along the lymph spaces of the lungs may be so extensive and the growth thereby excited be so great that the organs present the characters of a generalized interstitial inflammation. Neverthless, the distinction between local and general is in the main useful and not pedantic.

To turn now to the replacement fibroses; among these we can distinguish certain well-defined types. All may in truth be termed cicatricial, but it may be well to restrict this designation to the ordinary surgical cicatrix, to the connective tissue developed after breach of continuity in a part. Speaking broadly, it may be said that every such breach of continuity results in the destruction of a certain number of cells, and that in the absence of infective agents the new connective-tissue formation maintains a definite relationship to the amount of previous destruction, never exceeding it. Very closely allied is the development following upon the complete and sudden necrosis of all the elements of a tissue; of this, as previously hinted, a most satisfactory example is seen in the healing of a simple infarct.

If we, following what is not unusual nowadays, regard the blood as a tissue, the organization of thrombi must be placed under the same heading of fibrosis following tissue necrosis; if we are more conservative in our employment of the term "tissue," we must regard the gradual substitution of the coagulated and necrosed blood by fibrous tissue as a closely allied phenomenon, namely as a fibrosis occurring in and replacing a necrotic mass.

Associated with these we can recognize two other forms. I would not insist upon their separation, but there is a slight difference in their mode of origin. In the one the essential cause of the death of the cells is local, from impaired nutrition, in the other the nobler elements of the tissue undergo atrophy and death irrespective of local conditions. The two forms may be termed dystrophic and atrophic, respectively.

Of the atrophic I have already furnished an example, namely, the sclerosis following degeneration of ascending or descending nerve tracts. Of the dystrophic the heart furnishes the most frequent examples, though I am inclined to regard much of the fibroid change seen in the senile kidney as of the same nature. As M. H. Martin [1] was, I think, the first to point out explicitly, and as Weber [2] has shown in a very careful research, where there is an "obliterating endarteritis" of the coronary vessels with overgrowth of the intima and consequent diminution of the lumen, there must result a diminished nutrition of the area supplied by each affected artery or arteriole, and as these are of the nature of end arteries there is developed no satisfactory collateral nutrition. The result affords a very striking picture, more especially if the most frequent seat of the change be examined, namely, one of the papillary muscles of the left heart. In these the fibres run longitudinally and so also, entering at the base, do the nutrient arteries, and the condition is so common that I have never had difficulty in obtaining material for my class in morbid histology. In a typical fairly advanced case in transverse section of the muscle, the arterioles with thickened intima are seen cut transversely; around each is a zone of fairly healthy fibres also cut transversely. Passing outward from the artery these give place to fibres that present atrophy and pigmental degeneration with intermingling of new connective tissue, while the outer zone of supply of the arteriole is represented by a ring of clear, transparent fibrous tissue with relatively few nuclei and here and there the last remnant of a degenerated muscle fibre. This, I may remark, is but one form of cardiac sclerosis. It would be difficult to find a more demonstrative case of this dystrophic replacement fibrosis.

But while thus we are able to recognize examples of the uncomplicated occurrence of one or other form of inflam-

[1] H. Martin: *Revue de Médecine*. May, 1881.

[2] A. Weber: *Contribution à l'Etude Anatomo-pathologique de l'Arterio-sclérose du Cœur*, Paris, Steinheil, 1887.

matory fibrosis, and while I hold that it is useful to us both as students of medical science and as practical physicians and surgeons to seek to analyze the nature and character of every morbid change, it has to be admitted, if we look honestly at things as they are, that case after case presenting itself to our notice cannot possibly be docketed and pigeonholed under one heading. Time and again we come across what can only be classified as mixed forms of the conditions already indicated, not to mention mixture of these with fibroid conditions which I have still to take into consideration. I can only urge that it is well to strive to cultivate our garden and not to allow our ideas of chronic inflammation to continue a riotous and tangled growth. Only by such cultivation can we hope to gain good fruit.

It is when we come to study the chronic inflammations affecting glandular organs that our great difficulty begins in comprehending the essential nature and causation of connective-tissue growth. Let us take the commonest case, namely, that of continued parenchymatous inflammation. Here the first obvious disturbance in the tissue is an affection of the glandular cells. With this there is an accompanying congestion of the interstitial vessels, and this gives place eventually to a condition in which the collections of gland cells are separated from each other by increased connective tissue, while coincidently the gland cells themselves show signs of atrophy. Two conditions might produce this picture: either the atrophy of the gland cells might be primary and the increased fibrous tissue an indication of replacement fibrosis; or, on the other hand, the picture might indicate, as is usually held, a productive interstitial fibrosis with the malnutrition and atrophy of the gland cells as a secondary consequence of irritation, impaired nutrition, and pressure exerted by the new-formed tissue combined. It is only by a very full and cautious observation that it is possible to arrive at a decision in any given case as to which form of fibrosis is represented and often, indeed, one is induced to take the middle course and consider both in operation.

If, for example, we study the various forms of cirrhosis of the liver both experimentally and by histological examination of various cases, this difficulty is very forcibly borne home to us. We can occasionally, it is true, make out with certainty the existence of a productive fibrosis; thus we frequently meet with what appears to be the earliest stage of ordinary so-called alcoholic cirrhosis, in which we observe small masses of small-celled infiltration along the portal sheaths. The condition looks definitely productive; it appears to be an inflammation around the interlobular branches of the portal vein, and the cells in the immediate neighborhood of these accumulations show no very decided signs of degeneration and atrophy. We can, again, as is occasionally the case in early stages of biliary obstruction, find the bile ducts enlarged and dilated and surrounded each with new connective tissue, so that the picture given is that of a productive inflammation immediately around these ducts. We can also, more frequently than is usually recognized, make out signs of fibrous-tissue overgrowth around the branches of the hepatic artery; out of eighty-eight post-mortems performed during last year, I found this periarteritis to be well marked in six cases; but in advanced cases of ordinary cirrhosis of the atrophic type it seems to me more than doubtful whether malnutrition of the cell does not become an important factor and their atrophy be not followed by replacement fibrosis, rather than be the result of pressure and encroachment of the newly developed connective tissue.

In this connection it is interesting to note how the majority of observers who have attempted experimentally to induce cirrhosis of the liver have noticed changes of a degenerative character in the hepatic cells as a first effect of irritation rather than productive inflammation in the interstitial substance. This, of course, is what might be expected, the nobler cells of the tissue being the more sensitive. I merely draw attention to it because it is so common to regard hepatic cirrhosis as primarily an inter-

stitial disturbance. I do not wish to give the impression that this may not be so in certain cases; very frequently, I feel assured, it is not. I need but remind you how strongly the recent studies by Flexner [1] uphold this view.

Here I may briefly refer to certain studies which have occupied me during the last two years upon the causation and nature of a very remarkable disease affecting the cattle in a limited region of Nova Scotia, the so-called Pictou cattle disease. I do not wish here to publish a detailed and circumstantial account of my observations, for to do so would not be just to Professor Welch, to whom I have promised my completed paper upon the subject. I may, however, repeat what is stated in my reports to the Dominion Government, namely, that the disease is of an infectious nature and due to a minute bacillus, characterized, as are so many of the pathogenic micro-organisms of lower animals by an intense polar staining, so that frequently it has the appearance of a diplococcus rather than of a bacillus.

The disease is apparently of slow onset; the affected cattle eventually suffer from an abundant dark-colored diarrhœa, present a moderate amount of ascites, fail to give milk, and then the end is ushered in either by a condition of violent excitement or by progressive muscular weakness.

At the post-mortem the most characteristic features are the ascites, a remarkable submucous œdema of portions of the intestine (I have seen similar submucous œdema in cirrhosis of the liver in man), enlargement of the abdominal lymphatic glands, and a very extensive cirrhosis of the liver.

It is in the lymph glands and the hepatic cells that the bacilli are present in greatest abundance.

The cirrhosis is generalized and of the pericellular type, and if the livers from a large number of cases be examined, the earliest stages would appear to be those of swelling and vacuolation of the hepatic cells, with great irregularity in the size of the nuclei. There may be great congestion of the hepatic (venous) capillaries, but this is unaccompanied

[1] Flexner: *Medical News* (Phila.), ii., 1894, p. 116.

by any notable small-celled infiltration. Following upon this stage of swelling, the hepatic cells undergo atrophy, sundry lobules and portions of the liver showing the process at a more advanced stage than do other portions. And this process may be so extensive that over large areas of the organ only isolated liver cells or clumps of three or four degenerating cells are to be recognized. With this the organ is not diminished, indeed the edges often tend to be slightly rounded and full; there is replacement of the degenerating cells and lobules by a delicate, somewhat œdematous, connective tissue. A characteristic of this new tissue is the relative absence of the ordinary signs of productive inflammation in the shape of small round cells. Of these there are a few, but very few; more frequent are small irregular cells, evidently degenerated liver cells, and others of the "spider-cell" variety, with fairly numerous delicate processes.

In short, the impression gained by studying numerous sections obtained from many animals dying in different stages is that there is here a primary irritation or overstimulation of the hepatic cells by the bacilli, followed by an atrophy of the same and coincident replacement fibrosis. I will not say that this replacement fibrosis is the only form of connective-tissue hyperplasia present in these cases; there are occasional indications of productive change. But it is, I feel assured, the main form present.

This generalized pericellular cirrhosis is, of course, not strictly comparable with the more usual forms of hepatic cirrhosis met with in the human being. Its interest lies in this, that occasionally, more especially in children, we observe a curiously similar condition of the liver without any clear evidence of syphilis, and in children also the victims of congenital syphilis, even as to a less extent in adults presenting tertiary syphilis, we are apt to meet with a more or less extensive pericellular cirrhosis. In such cases it may well be that the cirrhosis is of like origin, due, that is to say, to the direct irritation of the hepatic cells by pathogenic

bacteria or their products, to the atrophy of these cells and their replacement by delicate connective tissue.

Thus far, therefore, we have been able to recognize the following forms of fibrosis of inflammatory origin:

A. "Productive" fibroses.
   (1) Localized { focal. / capsular.
   (2) Serous and adhesive { local. / general.
   (3) Interstitial.
B. "Replacement" fibroses.
   (1) Cicatricial.
   (2) (Post)-necrotic.
   (3) (Post)-atrophic.
   (4) (Post)-dystrophic.
C. Mixed fibroses.

But this classification does not nearly include all the examples of connective-tissue overgrowth and sclerosis occurring in the organs of the body.

One further group of cases may at first sight appear to be sharply defined, namely, the group of the true fibroid neoplasms, the fibromata proper. Nevertheless, a study of the forms usually included in this group reveals the fact that there has been in the past not a little confusion as to what constitutes a fibroma, and an attempt to classify the various forms cannot but lead to the conclusion that the line separating inflammatory new formation from fibroid neoplasms be drawn only with a cautious hand.

As I have pointed out, one result of irritation may be overgrowth of connective tissue. Ordinarily this appears to be not greatly in excess of the needs of the injured area, nevertheless at times it exhibits itself greatly in excess of these needs. When infective agencies interfere with the normal course of cicatrization of a wound and the healing becomes delayed, when, in short, superadded to the normal tendency for fibrous tissue to be developed so as to repair a wound there is a stimulus to connective-tissue proliferation from the

presence of bacteria and their products, then it would appear that fibrous tissue may be developed in excess of the requirements of the part. This "false" cheloid, it is clear, originates primarily after inflammation, and we may have every gradation from what may be regarded without second thought as redundant cicatricial tissue up to what, from its continued and very extensive growth, it is difficult to regard as other than a frank neoplasm. Another form I have already referred to, namely, the "spontaneous" cheloid developing where there has been no breach of continuity of the tissues. On this continent among the colored population (and the negro appears to be peculiarly prone to be affected) cases have been recorded in which the new formation has attained enormous proportions.

As an example of so-called spontaneous cheloid let me here briefly describe the case already referred to, studied by Mr. R. Martin, for it throws light upon sundry important features in this class of tumors. The patient was a French Canadian girl, aged twenty, who had always been healthy until about four years ago, when she noticed a very small growth which looked like a little pimple on her left shoulder. This gradually enlarged and in about a year began to be painful, causing sharp, stinging pains. At the end of two years it was two inches long and three-quarters of an inch wide, and was then removed by the knife. About three weeks after the operation it recurred and became as large as before. An operation four months later was again followed by a recurrence. Three or four months later it was removed "by means of a plaster." It has never returned, but there remains a very large cicatrix, larger in fact than the original tumor. The patient was free from any further growths until about a year ago, when another small pimple appeared on the outer side of the right arm just above the elbow, which gradually grew larger until in April, 1895, it was one inch long, about a third of an inch wide, and elevated above the skin. The edges where it passed into the surrounding skin were irregular and claw-like. On further examination

another similar tumor was found on the back, and when the skin was made tense in several places, principally on the outer side of the right arm, clusters of flat, small round cicatricial spots were noted, of a white and glistening appearance. Each cluster contained about four or five spots. Upon relaxing the skin these clusters were unnoticeable. In July the clusters had all disappeared and there remained only the tumor on the back, which was also diminishing in size. At this time needle scratches were made on the left arm. When seen again in September, 1895, little nodular lines of cicatricial aspect were to be observed corresponding to the previous slight scratches caused by the needle. It may be added that microscopical examination of the tumor removed from the arm in April presented all the characters of true cheloid.

Here, then, we have a case apparently of spontaneous cheloid, in which nevertheless the subsequent history, results of operation, and of experimental slight cutaneous disturbance show that the fibroid hyperplasia was to be induced by injury, so that presumably the primary growth had a similar origin, not improbably, as in certain recorded cases, from an acne pustule. The case affords an example of what might very easily in its earlier stages have been classified as spontaneous cheloid.

In fact, from this case and from a study of the literature of cheloid, I am led with Jonathan Hutchinson to doubt whether the conception of a spontaneous cheloid is possible or consonant with facts.

Thus, it can be shown that in those exhibiting a tendency to the disease—those in whom cheloid masses already exist—a minimal irritation as, for example, the scratch of a pin, may induce the subsequent appearance of a mass of subcutaneous fibrous tissue in the region. Where this is the case it is difficult to deny that the condition originates as a productive inflammatory fibrosis, and the fact that at times some if not all of the multiple nodules undergo absorption and disappear (as happened in Mr. Martin's case to which I have

already referred) is against regarding the condition as typically fibromatous. It is equally difficult, in fact impossible, to maintain that a mass of new tissue, which occasionally attains to the weight of a pound or more, projecting from the head or trunk is an example of inflammatory fibrosis. It is difficult to see where the line is to be drawn, unless, as I have recently urged in an address before the Medico-Chirurgical Society at Montreal,[1] we recognize that in inflammation the new-tissue formation ceases with the removal or cessation of the irritant, whereas in neoplasms the cells, having once commenced to proliferate rapidly (whether as the result of chronic inflammation of moderate intensity or from other cause or causes), gain a habit of growth and continue to proliferate independently of any due stimulus. Assuredly, in these multiple cheloids as in the cicatricial forms growth of the tissue is continued after the irritant has ceased to be in evidence, and consequently I am bound from their course to classify them as among the fibromata—as fibromata of inflammatory origin.

I am not prepared to do the same with another form, the so-called "lamella fibromata," whereof the most frequent examples are to be encountered as dense, sharply defined, whitish nodules and small plaques upon the surface of the spleen. So far as I have been able to follow their development, these appear to be examples of pure and simple inflammatory growth. I can see in them no evidence of continued growth independent of injury or irritation.

Besides these two forms we have the group of typical fibromata, isolated, sharply defined neoplasms of in general slow growth. While among the cheloids we can postulate an inflammatory origin, in these we cannot as yet venture to assign a satisfactory causation. Nor is the time quite ripe to make a positive statement concerning the massive interstitial tissue occurring in sundry mixed tumors, in fibrolipomata, fibromyxomata, scirrhous cancer, etc. Studying these and comparing the outer border with the more internal parts,

[1] "The Habit of Growth," Montreal *Medical Journal*, February, 1896.

I gain the impression that in many cases we have, as in cheloid, to deal with a productive inflammatory fibrosis which merges insensibly into neoplastic incontinent growth. This is my impression, and I dare make no more definite statement.

Thus we can divide the forms contained under the title of fibroma into:

A. Pure or true fibroma.
   (1) Of inflammatory origin (most if not all examples of cheloid).
   (2) Of undetermined causation (typical hard and soft fibromata).

B. Mixed fibroma, benign, cancerous, and sarcomatous (admixture of fibroid overgrowth with overgrowth of other tissues).

C. False fibroma (due to simple productive inflammation, *e. g.*, "lamellar" fibromata).

LECTURE II.

In my last lecture, having laid down my definition of inflammation—namely, that it is the series of changes constituting the local attempt at repair of injury or referred injury to a part,—I proceeded to discuss the forms of fibrous hyperplasia which in the terms of this definition might well be held to be of inflammatory origin, and showed or attempted to show that such forms might be divided into the two main classes of productive and replacement fibrosis. Following upon this, I discussed the group of localized neoplastic fibrous hyperplasias, and pointed out that two groups might be recognized: the neoplasms of inflammatory origin and those of as yet undetermined causation—the true fibromata.

A consideration of neoplastic growth leads almost insensibly to the inquiry whether it is requisite that injury should precede new connective-tissue formation. The answer must, I think, be an unhesitating No.

In the nobler tissues of the body we know full well that increased work leads to hypertrophy or, more correctly, to

hyperplasia; that is to say, a physiological stimulus leads to multiplication of the cell elements. What are the exact steps whereby this is brought about must perhaps always remain a matter of supposition, the most that we can say being that the call for increased work is followed by increased blood flow to the part with presumably increased nutrition, and that the increased work necessitates greater activity and increased metabolism in the individual cells. In connection with the basal connective tissue of the body it is difficult to grasp the idea of active work; to attempt to formulate such an idea may perhaps justly lay me open to the charge of dealing in transcendental pathology, and yet, as I shall proceed to show, a consideration of several forms of fibrous-tissue hyperplasia in connection with the different organs and diverse in character, forms in which it is difficult to decide any clear inflammatory origin, leads to the conclusion that there is a certain bond of union between them, that in them the existence of an increased strain upon the tissue is to be recognized, and that if we could group them together as being of the nature of "functional" hyperplasias or hyperplasias of increased function, we should advance materially in our grasp and comprehension of the same.

I had at one time thought that increased nutrition would be sufficient to explain these cases, and indeed I have been inclined to press this point until quite recently. It is certainly true (as is best shown by the cases of dystrophic sclerosis already mentioned) that a nutrition insufficient for the nobler elements of an organ suffices often for the active growth of connective tissue. This fact that a nutrition ample and suitable for one tissue does not suffice for another has long attracted attention, while the converse, or rather the corollary, was proved more than a century ago by John Hunter in his classical experiment of grafting the scantily nourished cock's spur upon the cock's comb, and in this richly vascular and well-nourished area obtaining a remarkable, if temporary, hypertrophy of the grafted organ. Under certain conditions, then, active increase of nutrition

of a part may lead to hyperplasia of its cells. Where the specific cells of a tissue undergo atrophy it may well be that there results a definite increase in the amount of nutritive fluid at the disposal of the baser interstitial cells, and that this has to be taken into consideration as well as any more direct stimulus to proliferation afforded by the products of tissue degeneration.

If this be so we are met with the likelihood that in conditions tending to altered nutrition of a part—leading to the tissues becoming bathed with lymph, either in excess of the needs of the specific and nobler cells of that tissue or of a quality not suited for the uses of those cells—there may be induced an overgrowth of connective tissue, a fibrosis, to be ascribed primarily to nutritional disturbances; or, in other words, it becomes likely that there may be nutritional fibroses as distinguished from inflammatory. Plausible as this seems, a fuller study of those cases which at first appear to be examples of simple nutritional fibrous overgrowth leads to the conviction that there is some further factor also at work. Or otherwise, increased nutrition, even if long-continued, does not inevitably lead to increased connective-tissue overgrowth, and therefore when we find this factor most in evidence in the production of any form of fibrosis we are bound to assume that there must be some additional directive factor. What I mean will best be shown by a study of the cases I am about to bring before you.

Take in the first place chronic obstruction to the flow of lymph. Where such obtains—whether by pressure of tumors upon the main lymph channels of a part, by blocking of the same, or by diseased states of the lymph glands—it is a matter of frequent observation that in the absence of satisfactory collateral tracts the part becomes swollen and gradually the fluid swelling gives place to a generalized, if not very extreme, connective-tissue overgrowth. In such cases the circulation of the blood through the affected area is maintained, there are no positive signs of inflammation evident either macroscopically or microscopically. We can-

not recognize in the condition an attempt at repair. The primary injury has been at a distance from the region of fibrosis. Nevertheless, it may be argued that the stagnating lymph acts in these cases as an irritant to the connective-tissue cells and that the condition must be regarded as a productive inflammatory fibrosis.

While this view deserves full consideration, its acceptance must lead us almost inevitably to a point at which we become bound to regard as of inflammatory origin every condition of fibroid overgrowth, whatever be the stimulus. Some limit, I think, must be given to our conception of what is included in the process. It will be seen that thus far every example given by me until the present case has been strictly within the limits of the definition laid down, namely, it has been reparative in its tendency and has been due to evident injury to the part which becomes the seat of the fibroid change. We must, I take it, decline to consider a lesion as an inflammatory fibrosis in the development of which these two conditions cannot be clearly recognized.

Failing inflammatory origin, can we regard the example given above as being brought about by perverted nutrition pure and simple? I am inclined to think that we cannot. We should expect perverted nutrition to tell first upon other and higher tissues, but in many of these cases we find singularly little evidence of primary degeneration of nobler tissues (the muscles and skin of an affected extremity, for example). Where the circulation of healthy blood persists through such a region there must occur constant interchange between blood and lymph, and the blood must carry away the products of tissue change to a considerable extent. Indeed we know that it is capable of vicariously removing much of the lymphatic fluid. With our present knowledge, all that it is absolutely safe to say is that we are here dealing with a quantitative disturbance in the lymph of the region, coupled with a mechanical disturbance, namely, increased extravascular and interstitial pressure; or, to put it otherwise, the cells of the connective tissue are subjected to an

altered tension. The qualitative disturbance is of doubtful extent.

With these cases of obstructed lymph flow in a part certain examples of elephantiasis Arabum would appear to be classed—provisionally. So little has been accomplished in establishing the real nature of this disease, or more truly of this group of diseases, that the most I dare venture to say is that disturbed outflow of lymph from the affected region seems to be in operation in some cases (elephantiasis lymphangiectatica), while others present indications of venous disturbance (elephantiasis telangiectodes); others again (the neuromatous and lipomatous forms) can only safely be described as hypertrophic conditions approaching peculiarly close to generalized neoplastic formation.

Without discussing further the intimate nature of the fibrous hyperplasia in these cases at the present time, let me pass on to consider another class of cases. Increased bathing of the tissue with lymph and increased lymph tension may also result from active and from passive hyperæmia. From either of these causes there may be passage outward of lymph from the blood-vessels in amount exceeding the efferent capacity of the lymphatics. Here again mere increased amount of lymph does not seem to lead necessarily to fibrosis. Some other factor or factors must be invoked. Thus in the liver, while extreme congestion leads especially to dilatation of the vessels with pressure atrophy of the specific cells, and though presumably there is here increased exudation, we get little evidence of fibrosis; long-continued moderate congestion induces, on the other hand, a very evident fibrosis, most marked, it is true, in the walls of and immediately around the intralobular branches of the hepatic vein, but seen also in the interstitial substance of the neighborhood. The peculiar arrangement of the new fibrous tissue shows that it cannot be regarded simply as an example of replacement fibrosis. The history in these cases points to the long-continued action of two factors—increased effusion of a not greatly altered lymph and long-continued (and

probably varying) pressure affecting especially the central parts of the lobule.

The relative rarity and the slight extent of the fibrous hyperplasia accompanying well-marked passive congestion is in itself an indication that the quality of the effused lymph plays a part in the development of the hyperplasia. Neither increased amount of lymph of poor quality in a part nor increased interstitial tension alone, it would seem, is capable of inducing overgrowth.

From this brief and hasty consideration of fibroid changes associated with the lymphatic and venous systems which are not to be regarded as of inflammatory origin, I will now pass on to discuss in somewhat greater detail what appear to me to be allied conditions affecting the heart and arterial system.

In ordinary practice apart from malformations, neoplasms, and the direct effects of trauma, the pathological changes of the heart valves are divided into the two broad classes of acute and chronic endocarditis, and although the non-committal name of arterio-sclerosis is in frequent use and although its employment appears to indicate a doubt as to the exact etiology of the condition, it must, I think, be admitted that such arterio-sclerotic changes are regarded as inflammatory in character, while sporadically the attempt is made to explain them by suggesting or presupposing the existence of some irritant substance in the blood which by direct action upon the vessel walls leads to injury and to reaction in the shape of connective-tissue overgrowth. I see, for example, that in a recent number of the *British Medical Journal* the apostle of uric acid, Dr. Haig, suggests that a cause for sclerosis of the heart valves is to be found in the irritant action of his beloved uric-acid crystals.[1]

The existence of inflammation as a cause of sclerosis is more frequently to be determined in connection with the

[1] Alexander Haig: "Arthritis and Endocarditis Due to Drugs which Diminish the Solvent Power of the Blood for Uric Acid," *British Medical Journal*, December 28, 1895.

heart valves than with the arterial intima. Thus, it is well recognized that acute valvular disease may be followed by chronic thickening of one or more segments, that similar thickening may follow rupture of a segment, and that a valvule which has from any cause become injured, whether from simple roughening of its surface or more usually from the development upon it of vegetations, may by friction induce inflammatory disturbances in the parts with which it comes into contact.

In general these forms present an irregular or varicose type of fibrosis, but it is often difficult, if not impossible, to distinguish from them sundry cases of chronic generalized thickening in which through degeneration localized disturbances have occurred in the thickened valves with, it may be, ulceration, deposit of fibrin, and subsequent organization. There are, that is to say, doubtful cases in which it is practically impossible to declare whether we are dealing with processes following upon localized valve lesions or with the sequelæ of a generalized lesion.

Apart from these undoubtedly the most common form of valve lesion met with in the post-mortem theatre is a generalized thickening. Perhaps generalized is not a wholly correct designation, for in the slightest forms it manifests itself more especially along the edges of the mitral segments, and in the aortic valvules it is below the line of apposition, and again at the insertion of each segment, that the fibrosis is most marked. So common is the condition that in general we disregard it and, accepting it as almost physiological, make no note thereof. But in the examination of a series of hearts we may pass almost imperceptibly from one case to another until we reach conditions of extreme mitral stenosis, with such extensive generalized thickening of the whole valve and consequent shortening of the new connective tissue laid down that the mitral veil becomes converted into a circular plate, or more generally into a short blunt funnel with button-hole passage. And we come across case after case of this category which shows no sign of localized

valvular disturbance either old or recent. The condition affects the whole of the valve and affects also the chordæ tendineæ, which are thickened and shortened.

While in acute endocarditis and in the nodose or verrucose sclerosis following upon such we find clear evidence of vascularization of the valves, and sections show fairly frequent vessels, this is not the case in the generalized thickening here referred to. The essential characteristic as revealed in sections is the rarity of the vessels; the fibrous tissue is laid down in layers parallel to the surface, and the most recent, the most cellular layers are those nearest to the endothelium—while the deepest layers, those most remote from the surface, show a peculiar tendency to degenerative changes. This tendency to hyaline swelling, fatty degeneration, and other evidences of necrobiosis—in short, to atheroma—is in itself a demonstration of lack of due vascularization and of malnutrition. Indeed, although I know that Luschka and others have described vessels throughout the extent of the mitral valve segments, my own injections of healthy hearts of several species have led me to the more generally accepted conclusion that the outer two-thirds of the mitral are almost, of the aortic valves are quite, non-vascular, and to the further conclusion that healthy valvules gain their nutrition in the main from the blood circulating within the heart. It is, I hold, by passage or circulation of the plasma through the stomata of the lining endothelial cells into the lymph spaces between the layers of connective tissue forming the supporting frame of each normal valvule that the main nutrition of the non-vascular areas of the valves is effected. While a layer of the vascular myocardium is contained in the proximal third or so of the segments, the outer two-thirds is scarce anything but a fold of the endocardium.

That the endocardium of the heart in general gains its nourishment from the blood within the chambers and that the nourishing plasma may even extend for some little distance beyond, is very prettily shown in some cases of ad-

vanced sclerosis of the papillary muscles, which present complete fibroid metamorphosis of the central area of the pillars with a zone of healthy fibres all around the periphery immediately beneath the endocardium. These healthy fibres present no accompanying arteries; all the arterioles coursing up the papillary muscle may exhibit advanced proliferating endarteritis. The only and the obvious explanation why these peripheral fibres remain is that they have gained their nourishment through the endocardium.

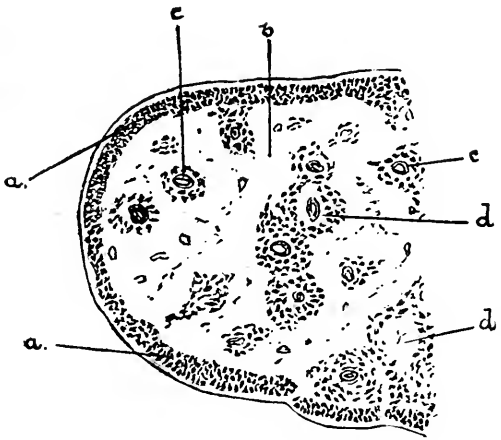

FIG. I.

Transverse section of a papillary muscle exhibiting dystrophic sclerosis to show zone of intact muscle fibres immediately beneath the endocardium. *a*, Layer of intact muscle fibres beneath endocardium; *b*, sclerosed areas—replacement of atrophied muscle tissue by fibrous tissue. In this are venules and occasional atrophied muscle fibres; *c*, arterioles cut tranversely, exhibiting thickened and sclerosed coats, and surrounded by intact muscle fibres; *d*, periarterial sclerosis.

Wherever we find well-marked vascularization of the outer two-thirds of the mitral valve, for example, we may feel assured that there has been inflammation present. The vascularization is strictly comparable to that obtaining in the cornea and other non-vascular areas, and indicates a development secondary to acute disturbance of the organ. In the generalized thickening to which I have referred one is struck by the peculiar rarity or almost complete absence of vessels

and by the fact that the hypertrophic fibroid tissue is laid down after the plan of the normal connective layers of the region. And while obviously the new growth is continuing and the newest tissue is situated immediately beneath the endothelium, we do not there recognize any characteristic presence of small round cells. The appearances in this region are those of an orderly hypertrophy.

Two hypotheses may be adduced to explain this state of affairs: Either that the sclerosis is of inflammatory origin, the result of an irritant mild in character, causing little reaction but acting continuously over a long period, or that it is non-inflammatory and comparable to the fibroses already referred to in connection with the lymphatic system.

It is, I must frankly confess, impossible to adduce sufficient proof to entirely refute the former hypothesis—there may be chronic intoxications, auto-intoxications, or otherwise, due to substances which manifest a special tendency to act upon the endocardium; but such substances have not yet been isolated. Increased pressure upon the valves may directly damage them and the fibrosis may be the indication of a reaction to chronic injury, but the thickening would appear to be progressive and to continue until a condition is reached out of all proportion to the injury. We find, therefore, no absolute and sufficient reason for regarding the condition as of inflammatory origin. Nevertheless, the mere fact that we at present are ignorant of any immediate cause for the production of this lesion is not sufficient ground for flatly denying the existence of such cause, and even the fact that the microscopic appearances are not those of ordinary inflammation is not proof positive that the process which has led to the lesion has not been essentially of an inflammatory nature.

I cannot, that is to say, hold it proved or disproved that generalized sclerosis of the cardiac valves is in all cases of inflammatory nature. And the matter being thus an open one, it may be well to hold it possible that the second alternative may be correct and to seek for evidence in support of it.

Now, it is interesting to note that just those conditions in which there is a liability for the production of generalized thickening of the heart valves are, clinically, conditions in which there is found heightened arterial tension, conditions which also bring about arterio-sclerosis. It is just in these conditions that we might expect to have, with increased pressure, increased nutrition of the endocardium and of the intima—increased passage of plasma from the intracardiac blood through the endothelium, or perhaps, more correctly, between the endothelial cells. And I cannot but consider that this increased nutrition coupled with increased strain may afford a satisfactory explanation for this condition of so-called chronic endocarditis. Such a proof as one would desire of the correctness of this opinion is difficult if not impossible to devise, for the condition is the production not of a few hours but, not to exaggerate, of many weeks. Experiments upon the subject are almost if not quite outside the range of experimental pathology. Yet certain considerations appear to support the view. Roy and I,[1] for example, found that by constricting the first part of the aorta in the dog and in the rabbit and thereby raising the blood pressure within the heart, we were able in the course of a few minutes to bring about the production of numerous small pearly vesicles along the edges of apposition of the mitral and aortic valves, and we could only account for this development by assuming that with the increased blood pressure the plasma of the blood had been driven into the substance of the valve, and that the pearly vesicles of lymph (or plasma) appeared where they did because at these regions the difference between the pressure on one side of the valve segments and on the other was most in evidence. We obtained, so we held, clear proof that with increased blood pressure increased fluid penetrates the valve substance. It is important to note that similar pearly elevations are generally regarded as the first indication of valve disease.

[1] Roy and Adami: "On Failure of the Heart from Overstrain," *British Medical Journal*, December 15, 1888.

But, as I have already pointed out, it is unsafe to regard increased nutrition alone as a cause of connective-tissue hypertrophy, and if we cast round to find what other factor there may be I am inclined to consider that it may briefly be entitled increased strain or tension acting upon the individual connective-tissue cells.

The idea may at first appear transcendental; we are not accustomed to think of the connective-tissue framework of the organism as being strained or, to carry this view to its logical conclusion, performing work. We only regard the nobler tissues as workers—the muscle fibres, the nerve cells and the specific cells of the glands. Nevertheless, we acknowledge freely that increased work thrown upon one of the connective tissues—namely, bone—does lead to its hypertrophy. It is a matter of common observation that not only are the bones of those accustomed to active exercise larger and heavier than the bones of the sedentary, but also that where any muscles are strongly developed there bony ridges and bony overgrowths are most developed at their origins and insertions.

The factors leading to this overgrowth may be summed up under the comprehensive title of increased work. And in connection with connective tissue where there is any force in action tending to draw apart and pull upon the constituents of the tissue—whether the force acts from without or (as in cases of increased effusion of lymph) from within the tissue—where, in short, there is a strain upon the components of the tissue—there, if we regard the work of the connective tissues, as is most plausible, as being to bind together and support other tissues, undoubtedly that work is increased and, granting that at the same time the nutrition remains good, we have a condition favorable to increased growth. *A fortiori* we might expect such hypertrophy where simultaneously the amount of nutrition is increased.

I suggest this very tentatively, for I have a horror of far-fetched pathology and an accompanying belief that the fuller our knowledge of a subject the simpler and more

straightforward do we find the laws governing the associated phenomena, and it is only because the idea is straightforward and is in harmony with our knowledge of occurrences in connection with other tissues that I venture to formulate it. My aim in these lectures is throughout not to dictate but to suggest and call attention to the many diverse conditions which may bear a part in the production of increased fibrous tissue. At most I will here urge that it is possible that increased functional activity of the connective tissues results under favorable conditions in increased growth of the same.

Passing now to the arteries, we find that just as the muscular walls and pericardium of the heart are nourished by the coronary vessels, so the media and adventitia of the arteries are nourished by the vasa vasorum, whereas in health the intima appears to be non-vascular. Indeed, where it is well developed, the internal elastic lamina appears to constitute a boundary line between the vascular and non-vascular areas of the arteries. We are forced, I hold, to regard the intima as nourished from the blood circulating within the arteries.

The diseases to which the arterial walls are subject are closely comparable with those of the heart. There can, for example, be undoubted inflammation; we may even have collections of pus cells separating the intima from the media, although this is very rare and is always secondary to a purulent mesarteritis, the pus cells wandering into the intima from the vessels of the media. Even in cases of septic embolism or thrombosis, necrosis is the first noticeable change in the intima, and the invasion of leucocytes appears to be associated with the later inflammation of the media and adventitia. Rather more frequent is an acute productive inflammation, seen especially in the first portion of the aorta. This appears to be secondary to similar verrucose, subacute, and ulcerous inflammation of the aortic valvules. It is characterized by the development of almost papillomatous or warty processes projecting into the lumen of the

aorta, and these are richly cellular and also vascularized from the vasa vasorum. They are often covered by a layer of coagulum.

But these obviously inflammatory conditions are relatively rare. The most common form of arterial disease in the larger arteries is that termed by Virchow endarteritis chronica nodosa sive deformans, the arterio-sclerosis of Lobstein, or atheroma. I need not here enter into statistics concerning its frequency, or take up your time by details concerning the forms that it may assume. I will accept Dr. Councilman's classification,[1] simply modifying his terminology to indicate my doubts as to the endarteritic or inflammatory nature of the conditions. With him, therefore, I would distinguish (*a*) a nodular arterio-sclerosis, (*b*) senile arterio-sclerosis, and (*c*) diffuse arterio-sclerosis; and would with him acknowledge that these three forms merge one into the other. For our purpose as throwing light upon the nature of the condition, the nodular form, the true endarteritis nodosa of Virchow, is that to which I would more especially call your attention.

The process begins by the development of semi-transparent, almost gelatinous, plaques here and there upon the walls of the aorta and larger vessels, most often in the neighborhood of and around the orifice of some side branch. Where the process is older the plaques are found firm, dense and of almost cartilaginous hardness, and with this stage the deeper regions of the plaques exhibit manifest degenerative changes, passing on to the deposit of calcareous salts in the necrobiotic substance.

If we examine these plaques we are struck by the following peculiarities: (1) The endothelium over the plaque is continuous and apparently unaffected; (2) the new tissue is laid down regularly in layers parallel to the endothelium; (3) the connective tissue of the intima in the immediate neighborhood of the plaque passes imperceptibly into the

[1] Councilman: "On the Relations between Arterial Disease and Tissue Changes." *Trans. Association American Physician*, vi., 1891, p. 179.

hypertrophied connective tissue forming the plaque; there is no boundary line to be made out; (4) the oldest layers of the plaque are evidently those nearest to the elastic lamina, the most recent are beneath the endothelium and farthest away from the vasa vasorum of the media; and (5) the plaque is devoid of vessels save and except in those cases in which there is an evident attempt at the removal of the necrosed atheromatous material, and vessels penetrate into the atheromatous mass from the media in a manner comparable with their passage into a thrombus. Such passage, it will be recognized, is of purely secondary nature—the fibrous tissue has developed and undergone degeneration before it takes place.

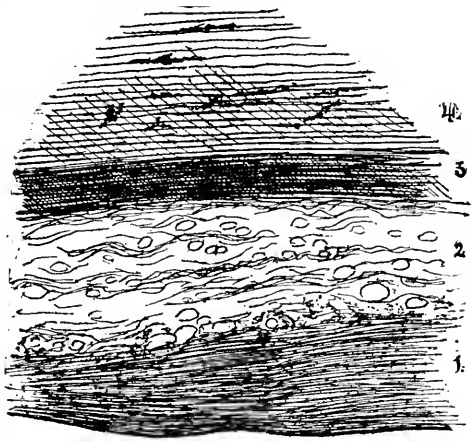

FIG. 2.

Section of the Aorta from a case of Nodose Arterio-sclerosis. 1, Thick layer of hyperplastic connective tissue lying immediately beneath the endothelium; 2, hyaline and fatty degeneration of the lower layers of the intima; 3, internal layers of the media, staining poorly and having a hyaloid appearance; 4, outer layers of the media—cellular infiltration around the vasa vasorum.[1]

The picture presented is not one usually associated with inflammation. The picture is rather what we should expect to find in an orderly connective-tissue hypertrophy, while

[1] For this specimen and that from which Fig. 3 has been made I am indebted to Dr. G. H. Mathewson, who is studying the cases of arterio-sclerosis occurring at the Royal Victoria Hospital, Montreal.

the degeneration appearing in the deeper layers is what might be expected to occur in a non-vascular area in which layer after layer of connective tissue cut off these deeper parts from their ordinary source of nutrition. Indeed, the sharp definition of the necrosed and calcareous tissue at the internal elastic lamina is often very remarkable and would appear not only to afford a proof of the correctness of the view that the intima is nourished from the interior of the artery, but also would suggest that the internal elastic lamina performs a very definite function in separating two vascular areas.

This, however, is not the whole picture. Constantly accompanying and indeed preceding the changes in the intima, there is to be recognized an injury or degeneration of the outer coats, whether of specific, inflammatory causation (as in cases recorded by Thoma and Peabody), or whether due to more obscure alterations in nutrition associated with disturbances of the vasa vasorum. In many cases these small vessels are congested and present either an infiltration of small round cells in their immediate neighborhood or the development of surrounding fibrous tissue. The muscle fibres of the media frequently exhibit hyaline and other degenerative changes, and there may be some replacement fibrosis, or again evidences of more extensive failure of nutrition and of necrobiosis in the shape of small areas of calcareous deposit. That is to say, the media is very definitely affected and, as Thoma's experiments have fully proved, each plaque of overgrowth of the intima corresponds to a localized giving way of the arterial wall, to a localized slight bulging of the same; for by injecting affected arteries with paraffin under a pressure of one hundred and sixty millimetres of mercury, Thoma obtained a smooth cylindrical mould showing no signs of depressions corresponding to any projecting plaques; the hypertrophied intima fills and obliterates the slight bulgings or pouches of the outer coats. However produced, there can be no question that we have here to deal with a compensatory hypertrophy of the intima.

In the diffuse form also Thoma has demonstrated that the growth of connective tissue in the intima has a similar compensatory nature.

Is this process to be denominated an inflammation?

Thoma and his pupils have shown that a thickening of the intima which they regard as strictly analogous is to be met with in the arteries of amputated limbs, in the portion of the aorta between the ductus Botalli and the offset of the umbilical arteries immediately following upon birth, in the uterine arteries after menstruation has set in, and still more clearly after childbirth; so to a less extent in the splenic arteries. All these latter cases must surely be classed among physiological rather than pathological reactions. Surely it is impossible to class a normal constant change, such as the overgrowth of the aortic intima following upon birth, as an inflammation. Nevertheless Thoma refers—or referred—to all these as conditions of compensatory endarteritis. But if he is right—and I do not see that he is not—in grouping all these cases, physiological and pathological, into one common class and ascribing to all a common causation, then not one ought strictly to be regarded as of inflammatory origin.

Thoma would explain his compensatory endarteritis according to the following law, namely, that the condition is to be ascribed to a slowing of the blood current. If this slowing be not arrested by a contraction of the media and consequent narrowing of the artery, leading to more rapid flow, then there occurs a new growth in the intima which leads to the same end—causing the lumen to become narrowed and the current to be restored to its normal rate.

He thus holds, and in this we must agree with him, that the primary lesion in arterio-sclerosis is a defect, a giving way, of the media, due to loss of elasticity however produced—and the only factor that he judges capable of explaining both the physiological and the pathological cases of connective-tissue overgrowth in the intima, and which is common to all cases, is relative slowing of the blood current. It is difficult to follow his explanation of the mechanism

whereby such slowing induces the hyperplasia of the fibrous tissue. Even if this slowing leads, as he indicates, to functional disturbance of the vasa vasorum, I cannot see how these vessels influence the nutrition of the intima. As I have said, I cannot find evidence that in healthy arteries or in the earlier stages of arterio-sclerosis any branches of these vessels pass into the intima. The process within the "bandelette" (as French histologists term the internal elastic lamina) appears to be at first sharply cut off from that occurring outside the same, and to be of a different nature—the new growth does not appear to develop from the neighborhood

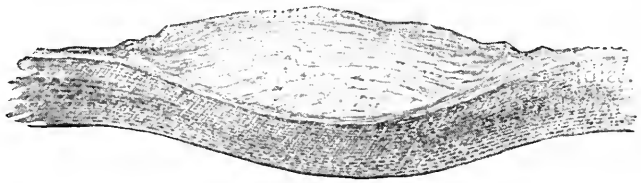

FIG 3.

Section of the Aorta from a case of Nodose Arterio-sclerosis, to show the bulging and thinning of the media, prepared by Dr. Mathewson; magnified 8 diameters. The section shows also the hyaline degeneration of the deeper layers of the overgrown intima, and the persistence of a fine layer of less altered intima tissue immediately beneath the media. The media in this case showed evidences of calcareous degeneration in patches, with some hyaline change.

of the "bandelette" and in the proximity of branches of the vasa vasorum entering the intima, did they exist (save, as I have already stated, secondarily to degenerative changes), but occurs at a region farthest away from such branches. At most a thin and in general hyaline degenerated layer may frequently be found lying between the calcified atheromatous mass in the overgrown intima and the internal elastic lamina. This would indicate that a small amount of nutrition is derived from the media. On the other hand, the examination of numerous sections would indicate that after the degeneration of the lower layers of the intima and the deposit there of a dense calcareous mass, growth still occurs actively and new layers become formed immediately beneath the endothelium. Were the main nutrition from the vasa vasorum of the media this would not be possible, and malnutrition

in consequence of disturbances in these vessels would lead to the production of wedges of degeneration extending toward the lumen, rather than to plaques of degeneration lying deep down in the thickened intima close to the internal elastic lamina.

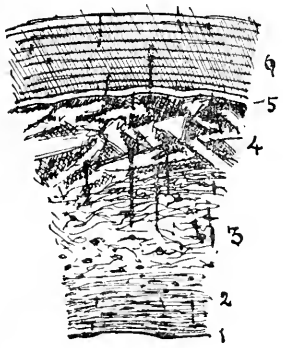

FIG. 4.

Section of an Artery of Medium Size, from the collection at McGill University. [This had been employed as a test specimen for the class and its label removed so that its exact origin cannot be stated.] 1, Intact endothelium; 2, layers of fibrous hyperplasia; 3, hyaline degeneration of the fibrous tissue; 4, layer of calcareous degeneration lying in immediate proximity to 5, the internal elastic lamina, somewhat swollen; 6, media presenting no distinct evidences of disease.

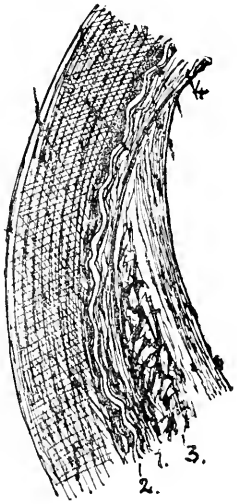

FIG. 5.

Section of Coronary Artery from a case of general Arterio-sclerosis, to show the persistence of a layer of but slightly altered connective tissue between the internal elastic lamina and the layer of calcareous degeneration. In this artery there had evidently been, as indicated at 4, two successive periods of sclerotic thickening of the intima, corresponding to a giving way of the media in two places.

Thus I cannot but conclude that disturbances in the vasa vasorum are incapable of immediately originating the changes that occur in the intima. There may be fibroid, hyaline, and necrotic changes in all the coats of an artery, but the sequence of changes in the intima does not maintain a strict dependence upon, and direct association with, the sequence in the media and adventitia.

Alterations in the vasa vasorum failing to explain the new growth, I am compelled to fall back upon altered tension as a factor to be adduced in partial explanation of these cases of increased growth. With Thoma we may possibly also call in the agency of the sensory and trophic nerves as governing the growth, but here we enter further upon speculative ground. They may play—they probably play—an active part, but we have no direct evidence that they do.

The most that we can safely urge is that with relative expansion of an artery, or portion of an artery, there must be an altered tension acting upon the cells of the intima of the affected region—that accepting the view that the intima is nourished from within the lumen, anything which will lead to increased passage of the blood plasma into the sub-endothelial layers of the intima may at the same time lead to an increased strain upon the connective-tissue cells of the intima, and so to increased proliferation of the same.

If this be so, we may have another ground than the histological appearance for regarding the condition as non-inflammatory; we have to deal with a stimulus rather than injury to the cells of the intima, and may see in the fibrous hyperplasia a response to a physiological stimulus rather than a reaction to injury. In any case, with our present knowledge, limited as it is, I would urge that the non-committal term of arterio-sclerosis is preferable to that of chronic endarteritis. Than this latter, the term chronic arteritis is more acceptable, for in connection with the artery as a whole as distinguished from the intima, there is, in the giving way and thinning of the media, evidence of injury, and in the intima as well as in the media, and it may be in the adventitia also, evidence of repair—of the artery as a whole, not of the intima; an arteritis, not an endarteritis.

The distinction, I admit, is finely drawn, yet I am compelled to acknowledge that it exists. I cannot acknowledge a physiological inflammation, and if, as Thoma points out, the initial process is identical in physiological overgrowth of the intima, and that occurring in arterio-sclerosis, then the

FIG. 6.

From a Section of the Left Ventricle of a patient dying from Aortic Stenosis with general Arterio-sclerosis, to show mixed dystrophic (*a*) and periarterial fibrosis (*d*).

latter process must be regarded as functional. Were some irritant discovered capable of directly inducing the hyperplasia of the intima, the case might present a different facies. That such an irritant exists is, it seems to me, highly improbable. The peculiar contrast between the pulmonary and the systemic arteries in their liability to arterio-sclerotic changes is strongly suggestive of the action of differences in the circulation as explaining the contrast, and not of the action of any irritative component of the blood.

I do but suggest this, and suggest it most tentatively. I shall feel rewarded if the suggestion leads to increased study into the phenomena underlying some of the commonest and most important forms of connective-tissue overgrowth. We are so wofully ignorant of the causation of such common conditions as chronic valve disease and arterio-sclerosis that I feel that, even if the views here enunciated originate strong and successful opposition, the stimulus they may have given to further investigation will be an ample reward.

The whole matter, as it appears to me, resolves itself into this: "Can we regard fibrous connective-tissue as following the same laws as the higher tissues, and so, as undergoing hypertrophy in consequence of increased work or increased strain brought to bear upon it?" If we can, then it would seem that we can divide off an important series of fibroses from the huge class of inflammatory fibroses. If we cannot, then we must continue to regard all fibroses save the neoplastic as chronic "itides."

Provisionally, therefore, I would divide the various forms of fibrosis as shown in the diagram, namely:

A. Of inflammatory origin:
   1. Replacement.
   2. Productive.
   3. Combined productive and replacement.
   4. Neoplastic.

B. Neoplastic, of undetermined causation
   1. True fibromata.

C. Of functional origin:

1. Lymphatic.
2. Venous.
3. Arterial.

There are very many individual cases of fibroid change that I have not discussed in these two lectures. To have done so would have consumed too much time and would have carried us still farther into conjectural regions. But the cases that I have brought before you represent, I believe, the main types of fibrosis; and those not here taken into consideration will, I believe, fall into one or other of the main classes here indicated.

In conclusion, I beg, Mr. President, to thank you and all the members for your great courtesy in enduring so patiently the long discourse that I have inflicted upon you, and once again to thank you for the honor you have conferred upon me in inviting me to deliver these lectures.

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